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(54) Title: METHODS OF DIAGNOSIS OF COLORECTAL CANCER, COMPOSITIONS AND METHODS OF SCREENING FOR COLORECTAL CANCER MODULATORS

(57) Abstract: Described herein are methods that can be used for diagnosis and prognosis of colorectal cancer. Also described herein are methods that can be used to screen candidate bioactive agents for the ability to modulate colorectal cancer. Additionally, methods and molecular targets (genes and their products) for therapeutic intervention in colorectal and other cancers are described.

Methods of Diagnosis of Colorectal Cancer, Compositions and Methods of Screening for Colorectal Cancer Modulators

CROSS-REFERENCES TO RELATED APPLICATIONS

[01] This application is a continuation in part of US Patent Application USSN 09/663,733 filed September 15, 2000, and US Patent Application filed August 14, 2001 USSN, not yet known, which are incorporated herein by reference in their entirety.

FIELD OF THE INVENTION

[02] The invention relates to the identification of expression profiles and the nucleic acids involved in colorectal cancer, and to the use of such expression profiles and nucleic acids in diagnosis and prognosis of colorectal cancer. The invention further relates to methods for identifying and using candidate agents and/or targets which modulate colorectal cancer.

BACKGROUND OF THE INVENTION

[03] Cancer of the colon and/or rectum (referred to as "colorectal cancer") are significant in Western populations and particularly in the United States. Cancers of the colon and rectum occur in both men and women most commonly after the age of 50. These develop as the result of a pathologic transformation of normal colon epithelium to an invasive cancer. There have been a number of recently characterized genetic alterations that have been implicated in colorectal cancer, including mutations in two classes of genes, tumor-suppressor genes and proto-oncogenes, with recent work suggesting that mutations in DNA repair genes may also be involved in tumorigenesis. For example, inactivating mutations of both alleles of the adenomatous polyposis coli (APC) gene, a tumor suppressor gene, appears to be one of the earliest events in colorectal cancer, and may even be the initiating event. Other genes implicated in colorectal cancer include the MCC gene, the p53 gene, the DCC (deleted in colorectal carcinoma) gene and other chromosome 18q genes, and genes in the TGF-β signaling pathway. For a review, see *Molecular Biology of Colorectal Cancer*, pp. 238-299, in *Curr. Probl. Cancer*, Sept/Oct 1997; see also Willams, *Colorectal Cancer* (1996); Kinsella & Schofield, *Colorectal Cancer: A Scientific Perspective* (1993); *Colorectal*

Cancer: Molecular Mechanisms, Premalignant State and its Prevention (Schmiegel & Scholmerich eds., 2000); *Colorectal Cancer: New Aspects of Molecular Biology and Their Clinical Applications* (Hanski *et al.*, eds 2000); McArdle *et al., Colorectal Cancer* (2000); Wanebo, *Colorectal Cancer* (1993); Levin, *The American Cancer Society: Colorectal Cancer* (1999); *Treatment of Hepatic Metastases of Colorectal Cancer* (Nordlinger & Jaeck eds., 1993); *Management of Colorectal Cancer* (Dunitz *et al.*, eds. 1998); *Cancer: Principles and Practice of Oncology* (Devita *et al.*, eds. 2001); *Surgical Oncology: Contemporary Principles and Practice* (Kirby *et al.*, eds. 2001); Offit, *Clinical Cancer Genetics: Risk Counseling and Management* (1997); *Radioimmunotherapy of Cancer* (Abrams & Fritzberg eds. 2000); Fleming, *AJCC Cancer Staging Handbook* (1998); *Textbook of Radiation Oncology* (Leibel & Phillips eds. 2000); and *Clinical Oncology* (Abeloff *et al.*, eds. 2000).

[04] Imaging of colorectal cancer for diagnosis has been problematic and limited. In addition, metastasis of the tumor to the lumen, and metastasis of tumor cells to regional lymph nodes are important prognostic factors (*see, e.g., PET in Oncology: Basics and Clinical Application* (Ruhlmann *et al.* eds. 1999). For example, five year survival rates drop from 80 percent in patients with no lymph node metastases to 45 to 50 percent in those patients who do have lymph node metastases. A recent report showed that micrometastases can be detected from lymph nodes using reverse transcriptase-PCR methods based on the presence of mRNA for carcinoembryonic antigen, which has previously been shown to be present in the vast majority of colorectal cancers but not in normal tissues. Liefers *et al., New England J. of Med.* 339(4):223 (1998).

[05] Thus, methods that can be used for diagnosis and prognosis of colorectal cancer would be desirable. Accordingly, provided herein are methods that can be used in diagnosis and prognosis of colorectal cancer. Further provided are methods that can be used to screen candidate bioactive agents for the ability to modulate colorectal cancer. Additionally, provided herein are molecular targets for therapeutic intervention in colorectal and other cancers.

BRIEF SUMMARY OF THE INVENTION

[06] The present invention provides novel methods for diagnosis and prognosis evaluation for colorectal cancer, as well as methods for screening for compositions which modulate colorectal cancer. Methods of treatment of colorectal cancer, as well as compositions, are also provided herein.

[07] In one aspect, a method of screening drug candidates comprises providing a cell that expresses an expression profile gene selected from those of Table I. The method further includes adding a drug candidate to the cell and determining the effect of the drug candidate on the expression of the expression profile gene.

[08] In one embodiment, the method of screening drug candidates includes comparing the level of expression in the absence of the drug candidate to the level of expression in the presence of the drug candidate, wherein the concentration of the drug candidate can vary when present, and wherein the comparison can occur after addition or removal of the drug candidate. In a preferred embodiment, the cell expresses at least two expression profile genes. The profile genes may show an increase or decrease.

[09] Also provided herein is a method of screening for a bioactive agent capable of binding to a colorectal cancer modulator protein, the method comprising combining the colorectal cancer modulator protein and a candidate bioactive agent, and determining the binding of the candidate agent to the colorectal cancer modulator protein. Preferably the colorectal cancer modulator protein is a product encoded by a gene of Table 1 or Table 2.

[10] Further provided herein is a method for screening for a bioactive agent capable of modulating the activity of a colorectal cancer modulator protein. In one embodiment, the method comprises combining the colorectal cancer modulator protein and a candidate bioactive agent, and determining the effect of the candidate agent on the bioactivity of the colorectal cancer modulator protein. Preferably the colorectal cancer modulator protein is a product encoded by a gene of Table 1 or Table 2.

[11] Also provided is a method of evaluating the effect of a candidate colorectal cancer drug comprising administering the drug to a transgenic animal expressing or over-expressing the colorectal cancer modulator protein, or an animal lacking the colorectal cancer modulator protein, for example as a result of a gene knockout.

[12] Additionally, provided herein is a method of evaluating the effect of a candidate colorectal cancer drug comprising administering the drug to a patient and removing a cell sample from the patient. The expression profile of the cell is then determined. This method may further comprise comparing the expression profile to an expression profile of a healthy individual. In a preferred embodiment, said expression profile includes a gene of Table 1 or Table 2.

[13] Moreover, provided herein is a biochip comprising one or more nucleic acid segments of Table 1 or Table 2, wherein the biochip comprises fewer than 1000 nucleic acid probes. Preferable at least two nucleic acid segments are included.

[14] Furthermore, a method of diagnosing a disorder associated with colorectal cancer is provided. The method comprises determining the expression of a gene of Table 1 or Table 2, in a first tissue type of a first individual, and comparing the distribution to the expression of the gene from a second normal tissue type from the first individual or a second unaffected individual. A difference in the expression indicates that the first individual has a disorder associated with colorectal cancer.

[15] In another aspect, the present invention provides an antibody which specifically binds to a protein encoded by a nucleic acid of Table 1 or Table 2 or a fragment thereof. Preferably the antibody is a monoclonal antibody. The antibody can be a fragment of an antibody such as a single stranded antibody as further described herein, or can be conjugated to another molecule. In one embodiment, the antibody is a humanized antibody.

[16] In one embodiment a method for screening for a bioactive agent capable of interfering with the binding of a colorectal cancer modulating protein (colorectal cancer modulator protein) or a fragment thereof and an antibody which binds to said colorectal cancer modulator protein or fragment thereof. In a preferred embodiment, the method comprises combining a colorectal cancer modulator protein or fragment thereof, a candidate bioactive agent and an antibody which binds to said colorectal cancer modulator protein or fragment thereof. The method further includes determining the binding of said colorectal cancer modulator protein or fragment thereof and said antibody. Wherein there is a change in binding, an agent is identified as an interfering agent. The interfering agent can be an agonist or an antagonist. Preferably, the agent inhibits colorectal cancer.

[17] In a further aspect, a method for inhibiting colorectal cancer is provided. The method can be performed in vitro or in vivo, preferably in vivo to an individual. In a preferred embodiment the method of inhibiting colorectal cancer is provided to an individual with cancer. As described herein, methods of inhibiting colorectal cancer can be performed by administering an inhibitor of the activity of a protein encoded by a nucleic acid of Table 1 or Table 2, including an antisense molecule to the gene or its gene product.

[18] Also provided herein are methods of eliciting an immune response in an individual. In one embodiment a method provided herein comprises administering to an individual a composition comprising a colorectal cancer modulating protein, or a fragment

thereof. In another embodiment, the protein is encoded by a nucleic acid selected from those of Table 1 or Table 2. In another aspect, said composition comprises a nucleic acid comprising a sequence encoding a colorectal cancer modulating protein, or a fragment thereof.

[19] Further provided herein are compositions capable of eliciting an immune response in an individual. In one embodiment, a composition provided herein comprises a colorectal cancer modulating protein, preferably encoded by a nucleic acid of Table 1 or Table 2, or a fragment thereof, and a pharmaceutically acceptable carrier. In another embodiment, said composition comprises a nucleic acid comprising a sequence encoding a colorectal cancer modulating protein, preferably selected from the nucleic acids of Table 1 or Table 2 and a pharmaceutically acceptable carrier.

[20] Also provided are methods of neutralizing the effect of a colorectal cancer protein, or a fragment thereof, comprising contacting an agent specific for said protein with said protein in an amount sufficient to effect neutralization. In another embodiment, the protein is encoded by a nucleic acid selected from those of Table 1 or Table 2.

[21] In another aspect of the invention, a method of treating an individual for colorectal cancer is provided. In one embodiment, the method comprises administering to said individual an inhibitor of a colorectal cancer modulating protein. In another embodiment, the method comprises administering to a patient having colorectal cancer an antibody to a colorectal cancer modulating protein conjugated to a therapeutic moiety. Such a therapeutic moiety can be a cytotoxic agent or a radioisotope.

[22] Compounds and compositions are also provided. Other aspects of the invention will become apparent to the skilled artisan by the following description of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[NOT APPLICABLE]

DETAILED DESCRIPTION OF THE INVENTION

[23] The present invention provides novel methods for diagnosis and prognosis evaluation for colorectal cancer, as well as methods for screening for compositions which modulate colorectal cancer. The methods herein are related to those of U.S. Patent Application Serial No. 09/525,993 and International Patent Application No. PCT/US00/07044, each of which is incorporated herein in its entirety.

[24] By "colorectal cancer" herein is meant a colon and/or rectal tumor or cancer that is classified as Dukes stage A or B as well as metastatic tumors classified as Dukes stage Cor D (*see, e.g.*, Cohen *et al.*, *Cancer of the Colon*, in *Cancer: Principles and Practice of Oncology*, pp. 1144-1197 (Devita *et al.*, eds., 5th ed. 1997); see also *Harrison's Principles of Internal Medicine*, pp. 1289-129 (Wilson *et al.*, eds., 12th ed., 1991). "Treatment, monitoring, detection or modulation of colorectal cancer" includes treatment, monitoring, detection, or modulation of colorectal disease in those patients who have colorectal disease (Dukes stage A , B, C or D) in which gene expression from a gene in Table 1 or 2, is increased or decreased, indicating that the subject is more likely to progress to metastatic disease than a patient who does not have an increase or decrease in gene expression of a gene in Table 1 or 2. In Dukes stage A, the tumor has penetrated into, but not through, the bowel wall. In Dukes stage B, the tumor has penetrated through the bowel wall but there is not yet any lymph involvement. In Dukes stage C, the cancer involves regional lymph nodes. In Dukes stage D, there is distant metastasis, e.g., liver, lung, etc.

[25] Table 1 provides unigene cluster identification numbers for the nucleotide sequence of genes that exhibit increased expression in colorectal cancer samples. Tables 1 also provides an exemplar accession number that provides a nucleotide sequence that is part of the unigene cluster. Table 2 provides the nucleic acid and protein sequence of the CBF9 gene as well as the Unigene and Exemplar accession numbers for CBF9.

[26] In one aspect, the expression levels of genes are determined in different patient samples for which either diagnosis or prognosis information is desired, to provide expression profiles. An expression profile of a particular sample is essentially a "fingerprint" of the state of the sample; while two states may have any particular gene similarly expressed, the evaluation of a number of genes simultaneously allows the generation of a gene expression profile that is unique to the state of the cell. That is, normal tissue may be distinguished from colorectal cancer tissue, and within colorectal cancer tissue, different prognosis states (good or poor long term survival prospects, for example) may be determined. By comparing expression profiles of colon tissue in known different states, information regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained. The identification of sequences that are differentially expressed in colorectal cancer versus normal colon tissue, as well as differential expression resulting in different prognostic outcomes, allows the use of this information in a number of ways. For example, the evaluation of a particular treatment regime may be evaluated: does a chemotherapeutic drug act to improve the long-term

prognosis in a particular patient. Similarly, diagnosis may be done or confirmed by comparing patient samples with the known expression profiles. Furthermore, these gene expression profiles (or individual genes) allow screening of drug candidates with an eye to mimicking or altering a particular expression profile; for example, screening can be done for drugs that suppress the colorectal cancer expression profile or convert a poor prognosis profile to a better prognosis profile. This may be done by making biochips comprising sets of the important colorectal cancer genes, which can then be used in these screens. These methods can also be done on the protein basis; that is, protein expression levels of the colorectal cancer proteins can be evaluated for diagnostic and prognostic purposes or to screen candidate agents. In addition, the colorectal cancer nucleic acid sequences can be administered for gene therapy purposes, including the administration of antisense nucleic acids, or the colorectal cancer proteins (including antibodies and other modulators thereof) administered as therapeutic drugs.

[27] Thus the present invention provides nucleic acid and protein sequences that are differentially expressed in colorectal cancer, herein termed "colorectal cancer sequences". As outlined below, colorectal cancer sequences include those that are up-regulated (i.e. expressed at a higher level) in colorectal cancer , as well as those that are down-regulated (i.e. expressed at a lower level) in colorectal cancer . In a preferred embodiment, the colorectal cancer sequences are from humans; however, as will be appreciated by those in the art, colorectal cancer sequences from other organisms may be useful in animal models of disease and drug evaluation; thus, other colorectal cancer sequences are provided, from vertebrates, including mammals, including rodents (rats, mice, hamsters, guinea pigs, etc.), primates, farm animals (including sheep, goats, pigs, cows, horses, etc). colorectal cancer sequences from other organisms may be obtained using the techniques outlined below.

[28] Colorectal cancer sequences can include both nucleic acid and amino acid sequences. In a preferred embodiment, the colorectal cancer sequences are recombinant nucleic acids. By the term "recombinant nucleic acid" herein is meant nucleic acid, originally formed in vitro, in general, by the manipulation of nucleic acid by polymerases and endonucleases, in a form not normally found in nature. Thus an isolated nucleic acid, in a linear form, or an expression vector formed in vitro by ligating DNA molecules that are not normally joined, are both considered recombinant for the purposes of this invention. It is understood that once a recombinant nucleic acid is made and reintroduced into a host cell or organism, it will replicate non-recombinantly, i.e. using the in vivo cellular machinery of the

host cell rather than in vitro manipulations; however, such nucleic acids, once produced recombinantly, although subsequently replicated non-recombinantly, are still considered recombinant for the purposes of the invention.

[29] Similarly, a "recombinant protein" is a protein made using recombinant techniques, i.e. through the expression of a recombinant nucleic acid as depicted above. A recombinant protein is distinguished from naturally occurring protein by at least one or more characteristics. For example, the protein may be isolated or purified away from some or all of the proteins and compounds with which it is normally associated in its wild type host, and thus may be substantially pure. For example, an isolated protein is unaccompanied by at least some of the material with which it is normally associated in its natural state, preferably constituting at least about 0.5%, more preferably at least about 5% by weight of the total protein in a given sample. A substantially pure protein comprises at least about 75% by weight of the total protein, with at least about 80% being preferred, and at least about 90% being particularly preferred. The definition includes the production of a colorectal cancer protein from one organism in a different organism or host cell. Alternatively, the protein may be made at a significantly higher concentration than is normally seen, through the use of an inducible promoter or high expression promoter, such that the protein is made at increased concentration levels. Alternatively, the protein may be in a form not normally found in nature, as in the addition of an epitope tag or amino acid substitutions, insertions and deletions, as discussed below.

[30] In a preferred embodiment, the colorectal cancer sequences are nucleic acids. As will be appreciated by those in the art and is more fully outlined below, colorectal cancer sequences are useful in a variety of applications, including diagnostic applications, which will detect naturally occurring nucleic acids, as well as screening applications; for example, biochips comprising nucleic acid probes to the colorectal cancer sequences can be generated. In the broadest sense, then, by "nucleic acid" or "oligonucleotide" or grammatical equivalents herein means at least two nucleotides covalently linked together. A nucleic acid of the present invention will generally contain phosphodiester bonds, although in some cases, as outlined below, nucleic acid analogs are included that may have alternate backbones, comprising, for example, phosphoramidate (Beaucage et al., Tetrahedron 49(10):1925 (1993) and references therein; Letsinger, J. Org. Chem. 35:3800 (1970); Sprinzl et al., Eur. J. Biochem. 81:579 (1977); Letsinger et al., Nucl. Acids Res. 14:3487 (1986); Sawai et al, Chem. Lett. 805 (1984), Letsinger et al., J. Am. Chem. Soc. 110:4470 (1988); and Pauwels et al., Chemica Scripta 26:141 91986)),

phosphorothioate (Mag et al., Nucleic Acids Res. 19:1437 (1991); and U.S. Patent No. 5,644,048), phosphorodithioate (Briu et al., J. Am. Chem. Soc. 111:2321 (1989), O-methylphophoroamidite linkages (see Eckstein, Oligonucleotides and Analogues: A Practical Approach, Oxford University Press), and peptide nucleic acid backbones and linkages (see Egholm, J. Am. Chem. Soc. 114:1895 (1992); Meier et al., Chem. Int. Ed. Engl. 31:1008 (1992); Nielsen, Nature, 365:566 (1993); Carlsson et al., Nature 380:207 (1996), all of which are incorporated by reference). Other analog nucleic acids include those with positive backbones (Denpcy et al., Proc. Natl. Acad. Sci. USA 92:6097 (1995); non-ionic backbones (U.S. Patent Nos. 5,386,023, 5,637,684, 5,602,240, 5,216,141 and 4,469,863; Kiedrowshi et al., Angew. Chem. Intl. Ed. English 30:423 (1991); Letsinger et al., J. Am. Chem. Soc. 110:4470 (1988); Letsinger et al., Nucleoside & Nucleotide 13:1597 (1994); Chapters 2 and 3, ASC Symposium Series 580, "Carbohydrate Modifications in Antisense Research", Ed. Y.S. Sanghui and P. Dan Cook; Mesmaeker et al., Bioorganic & Medicinal Chem. Lett. 4:395 (1994); Jeffs et al., J. Biomolecular NMR 34:17 (1994); Tetrahedron Lett. 37:743 (1996)) and non-ribose backbones, including those described in U.S. Patent Nos. 5,235,033 and 5,034,506, and Chapters 6 and 7, ASC Symposium Series 580, "Carbohydrate Modifications in Antisense Research", Ed. Y.S. Sanghui and P. Dan Cook. Nucleic acids containing one or more carbocyclic sugars are also included within one definition of nucleic acids (see Jenkins et al., Chem. Soc. Rev. (1995) pp169-176). Several nucleic acid analogs are described in Rawls, C & E News June 2, 1997 page 35. All of these references are hereby expressly incorporated by reference. These modifications of the ribose-phosphate backbone may be done for a variety of reasons, for example to increase the stability and half-life of such molecules in physiological environments or as probes on a biochip.

[31] As will be appreciated by those in the art, all of these nucleic acid analogs may find use in the present invention. In addition, mixtures of naturally occurring nucleic acids and analogs can be made; alternatively, mixtures of different nucleic acid analogs, and mixtures of naturally occurring nucleic acids and analogs may be made.

[32] Particularly preferred are peptide nucleic acids (PNA) which includes peptide nucleic acid analogs. These backbones are substantially non-ionic under neutral conditions, in contrast to the highly charged phosphodiester backbone of naturally occurring nucleic acids. This results in two advantages. First, the PNA backbone exhibits improved hybridization kinetics. PNAs have larger changes in the melting temperature (Tm) for mismatched versus perfectly matched basepairs. DNA and RNA typically exhibit a 2-4°C drop in Tm for an internal mismatch. With the non-ionic PNA backbone, the drop is closer to

7-9°C. Similarly, due to their non-ionic nature, hybridization of the bases attached to these backbones is relatively insensitive to salt concentration. In addition, PNAs are not degraded by cellular enzymes, and thus can be more stable.

[33] The nucleic acids may be single stranded or double stranded, as specified, or contain portions of both double stranded or single stranded sequence. As will be appreciated by those in the art, the depiction of a single strand ("Watson") also defines the sequence of the other strand ("Crick"); thus the sequences described herein also includes the complement of the sequence. The nucleic acid may be DNA, both genomic and cDNA, RNA or a hybrid, where the nucleic acid contains any combination of deoxyribo- and ribo-nucleotides, and any combination of bases, including uracil, adenine, thymine, cytosine, guanine, inosine, xanthine hypoxanthine, isocytosine, isoguanine, etc. As used herein, the term "nucleoside" includes nucleotides and nucleoside and nucleotide analogs, and modified nucleosides such as amino modified nucleosides. In addition, "nucleoside" includes non-naturally occurring analog structures. Thus for example the individual units of a peptide nucleic acid, each containing a base, are referred to herein as a nucleoside.

[34] A colorectal cancer sequence can be initially identified by substantial nucleic acid and/or amino acid sequence homology to the colorectal cancer sequences outlined herein. Such homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions.

[35] The isolation of mRNA comprises isolating total cellular RNA by disrupting a cell and performing differential centrifugation. Once the total RNA is isolated, mRNA is isolated by making use of the adenine nucleotide residues known to those skilled in the art as a poly (A) tail found on virtually every eukaryotic mRNA molecule at the 3'end thereof. Oligonucleotides composed of only deoxythymidine [olgo(dT)] are linked to cellulose and the oligo(dT)-cellulose packed into small columns. When a preparation of total cellular RNA is passed through such a column, the mRNA molecules bind to the oligo(dT) by the poly (A) tails while the rest of the RNA flows through the column. The bound mRNAs are then eluted from the column and collected.

[36] The colorectal cancer sequences of the invention can be identified as follows. Samples of normal and tumor tissue are applied to biochips comprising nucleic acid probes. The samples are first microdissected, if applicable, and treated as described above for the preparation of mRNA. Suitable biochips are commercially available, for example

from Affymetrix. Gene expression profiles as described herein are generated, and the data analyzed.

[37] In a preferred embodiment, the genes showing changes in expression as between normal and disease states are compared to genes expressed in other normal tissues, including, but not limited to lung, heart, brain, liver, breast, kidney, muscle, prostate, small intestine, large intestine, spleen, bone, and placenta. In a preferred embodiment, those genes identified during the colorectal cancer screen that are expressed in any significant amount in other tissues are removed from the profile, although in some embodiments, this is not necessary. That is, when screening for drugs, it is preferable that the target be disease specific, to minimize possible side effects.

[38] In a preferred embodiment, colorectal cancer sequences are those that are up-regulated in colorectal cancer ; that is, the expression of these genes is higher in colorectal carcinoma as compared to normal colon tissue. "Up-regulation" as used herein means at least about a 1.1 fold change, preferably a 1.5 or two fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred. All accession numbers herein are for the GenBank sequence database and the sequences of the accession numbers are hereby expressly incorporated by reference. GenBank is known in the art, see, e.g., Benson, DA, et al., Nucleic Acids Research 26:1-7 (1998) and http://www.ncbi.nlm.nih.gov/. In addition, these genes were found to be expressed in a limited amount or not at all in heart, brain, lung, liver, breast, kidney, prostate, small intestine and spleen.

[39] In a preferred embodiment, colorectal cancer sequences are those that are down-regulated in colorectal cancer ; that is, the expression of these genes is lower in colorectal carcinoma as compared to normal colon tissue. "Down-regulation" as used herein means at least about a two-fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred.

[40] Colorectal cancer proteins of the present invention may be classified as secreted proteins, transmembrane proteins or intracellular proteins. In a preferred embodiment the colorectal cancer protein is an intracellular protein. Intracellular proteins may be found in the cytoplasm and/or in the nucleus. Intracellular proteins are involved in all aspects of cellular function and replication (including, for example, signaling pathways); aberrant expression of such proteins results in unregulated or disregulated cellular processes. For example, many intracellular proteins have enzymatic activity such as protein kinase activity, protein phosphatase activity, protease activity, nucleotide cyclase activity,

polymerase activity and the like. Intracellular proteins also serve as docking proteins that are involved in organizing complexes of proteins, or targeting proteins to various subcellular localizations, and are involved in maintaining the structural integrity of organelles.

[41] An increasingly appreciated concept in characterizing intracellular proteins is the presence in the proteins of one or more motifs for which defined functions have been attributed. In addition to the highly conserved sequences found in the enzymatic domain of proteins, highly conserved sequences have been identified in proteins that are involved in protein-protein interaction. For example, Src-homology-2 (SH2) domains bind tyrosine-phosphorylated targets in a sequence dependent manner. PTB domains, which are distinct from SH2 domains, also bind tyrosine phosphorylated targets. SH3 domains bind to proline-rich targets. In addition, PH domains, tetratricopeptide repeats and WD domains to name only a few, have been shown to mediate protein-protein interactions. Some of these may also be involved in binding to phospholipids or other second messengers. As will be appreciated by one of ordinary skill in the art, these motifs can be identified on the basis of primary sequence; thus, an analysis of the sequence of proteins may provide insight into both the enzymatic potential of the molecule and/or molecules with which the protein may associate.

[42] In a preferred embodiment, the colorectal cancer sequences are transmembrane proteins. Transmembrane proteins are molecules that span the phospholipid bilayer of a cell. They may have an intracellular domain, an extracellular domain, or both. The intracellular domains of such proteins may have a number of functions including those already described for intracellular proteins. For example, the intracellular domain may have enzymatic activity and/or may serve as a binding site for additional proteins. Frequently the intracellular domain of transmembrane proteins serves both roles. For example certain receptor tyrosine kinases have both protein kinase activity and SH2 domains. In addition, autophosphorylation of tyrosines on the receptor molecule itself, creates binding sites for additional SH2 domain containing proteins.

[43] Transmembrane proteins may contain from one to many transmembrane domains. For example, receptor tyrosine kinases, certain cytokine receptors, receptor guanylyl cyclases and receptor serine/threonine protein kinases contain a single transmembrane domain. However, various other proteins including channels and adenylyl cyclases contain numerous transmembrane domains. Many important cell surface receptors are classified as "seven transmembrane domain" proteins, as they contain 7 membrane spanning regions. Important transmembrane protein receptors include, but are not limited to

insulin receptor, insulin-like growth factor receptor, human growth hormone receptor, glucose transporters, transferrin receptor, epidermal growth factor receptor, low density lipoprotein receptor, epidermal growth factor receptor, leptin receptor, interleukin receptors, e.g. IL-1 receptor, IL-2 receptor, etc.

[44] Characteristics of transmembrane domains include approximately 20 consecutive hydrophobic amino acids that may be followed by charged amino acids. Therefore, upon analysis of the amino acid sequence of a particular protein, the localization and number of transmembrane domains within the protein may be predicted.

[45] The extracellular domains of transmembrane proteins are diverse; however, conserved motifs are found repeatedly among various extracellular domains. Conserved structure and/or functions have been ascribed to different extracellular motifs. For example, cytokine receptors are characterized by a cluster of cysteines and a WSXWS (W= tryptophan, S= serine, X=any amino acid) motif. Immunoglobulin-like domains are highly conserved. Mucin-like domains may be involved in cell adhesion and leucine-rich repeats participate in protein-protein interactions.

[46] Many extracellular domains are involved in binding to other molecules. In one aspect, extracellular domains are receptors. Factors that bind the receptor domain include circulating ligands, which may be peptides, proteins, or small molecules such as adenosine and the like. For example, growth factors such as EGF, FGF and PDGF are circulating growth factors that bind to their cognate receptors to initiate a variety of cellular responses. Other factors include cytokines, mitogenic factors, neurotrophic factors and the like. Extracellular domains also bind to cell-associated molecules. In this respect, they mediate cell-cell interactions. Cell-associated ligands can be tethered to the cell for example via a glycosylphosphatidylinositol (GPI) anchor, or may themselves be transmembrane proteins. Extracellular domains also associate with the extracellular matrix and contribute to the maintenance of the cell structure.

[47] Colorectal cancer proteins that are transmembrane are particularly preferred in the present invention as they are good targets for immunotherapeutics, as are described herein. In addition, as outlined below, transmembrane proteins can be also useful in imaging modalities.

[48] It will also be appreciated by those in the art that a transmembrane protein can be made soluble by removing transmembrane sequences, for example through recombinant methods. Furthermore, transmembrane proteins that have been made soluble

can be made to be secreted through recombinant means by adding an appropriate signal sequence.

[49] In a preferred embodiment, the colorectal cancer proteins are secreted proteins; the secretion of which can be either constitutive or regulated. These proteins have a signal peptide or signal sequence that targets the molecule to the secretory pathway. Secreted proteins are involved in numerous physiological events; by virtue of their circulating nature, they serve to transmit signals to various other cell types. The secreted protein may function in an autocrine manner (acting on the cell that secreted the factor), a paracrine manner (acting on cells in close proximity to the cell that secreted the factor) or an endocrine manner (acting on cells at a distance). Thus secreted molecules find use in modulating or altering numerous aspects of physiology. colorectal cancer proteins that are secreted proteins are particularly preferred in the present invention as they serve as good targets for diagnostic markers, for example for blood tests.

[50] A colorectal cancer sequence is initially identified by substantial nucleic acid and/or amino acid sequence homology to the colorectal cancer sequences outlined herein. Such homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions.

[51] As used herein, the terms "colorectal cancer nucleic acid", "colorectal cancer protein" or "colorectal cancer polynucleotide" or "colorectal cancer-associated transcript" refers to nucleic acid and polypeptide polymorphic variants, alleles, mutants, and interspecies homologs that: (1) have a nucleotide sequence that has greater than about 60% nucleotide sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or greater nucleotide sequence identity, preferably over a region of over a region of at least about 25, 50, 100, 200, 500, 1000, or more nucleotides, to a nucleotide sequence of or associated with a unigene cluster of Tables 1 or Table 2; (2) bind to antibodies, e.g., polyclonal antibodies, raised against an immunogen comprising an amino acid sequence encoded by a nucleotide sequence of or associated with a unigene cluster of Table 1 or Table 2, and conservatively modified variants thereof; (3) specifically hybridize under stringent hybridization conditions to a nucleic acid sequence, or the complement thereof of Table 1 or Table 2 and conservatively modified variants thereof or (4) have an amino acid sequence that has greater than about 60% amino acid sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or greater amino sequence identity, preferably over a region of over a region of at least about

25, 50, 100, 200, 500, 1000, or more amino acid, to an amino acid sequence encoded by a nucleotide sequence of or associated with a unigene cluster of Table 1 or Table 2. A polynucleotide or polypeptide sequence is typically from a mammal including, but not limited to, primate, e.g., human; rodent, e.g., rat, mouse, hamster; cow, pig, horse, sheep, or other mammal. A "colorectal cancer polypeptide" and a "colorectal cancer polynucleotide," include both naturally occurring or recombinant.

[52] Homology in this context means sequence similarity or identity, with identity being preferred. A preferred comparison for homology purposes is to compare the sequence containing sequencing errors to the correct sequence. This homology will be determined using standard techniques known in the art, including, but not limited to, the local homology algorithm of Smith & Waterman, Adv. Appl. Math. 2:482 (1981), by the homology alignment algorithm of Needleman & Wunsch, J. Mol. Biool. 48:443 (1970), by the search for similarity method of Pearson & Lipman, PNAS USA 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Drive, Madison, WI), the Best Fit sequence program described by Devereux et al., Nucl. Acid Res. 12:387-395 (1984), preferably using the default settings, or by inspection.

[53] In a preferred embodiment, the sequences which are used to determine sequence identity or similarity are selected from the sequences set forth in Table 1 or Table 2. In one embodiment the sequences utilized herein are those set forth in Table 1 or Table 2. In another embodiment, the sequences are naturally occurring allelic variants of the sequences set forth in Table 1 or Table 2. In another embodiment, the sequences are sequence variants as further described herein.

[54] The terms "identical" or percent "identity," in the context of two or more nucleic acids or polypeptide sequences, refer to two or more sequences or subsequences that are the same or have a specified percentage of amino acid residues or nucleotides that are the same (i.e., about 60% identity, preferably 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity over a specified region, when compared and aligned for maximum correspondence over a comparison window or designated region) as measured using a BLAST or BLAST 2.0 sequence comparison algorithms with default parameters described below, or by manual alignment and visual inspection (*see, e.g.,* NCBI web site http://www.ncbi.nlm.nih.gov/BLAST/ or the like). Such sequences are then said to be "substantially identical." This definition also refers to, or may be applied to, the compliment of a test sequence. The definition also includes sequences that have deletions

and/or additions, as well as those that have substitutions, as well as naturally occurring, e.g., polymorphic or allelic variants, and man-made variants. As described below, the preferred algorithms can account for gaps and the like. Preferably, identity exists over a region that is at least about 25 amino acids or nucleotides in length, or more preferably over a region that is 50-100 amino acids or nucleotides in length.

[55] For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are entered into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. Preferably, default program parameters can be used, or alternative parameters can be designated. The sequence comparison algorithm then calculates the percent sequence identities for the test sequences relative to the reference sequence, based on the program parameters.

[56] A "comparison window", as used herein, includes reference to a segment of one of the number of contiguous positions selected from the group consisting typically of from 20 to 600, usually about 50 to about 200, more usually about 100 to about 150 in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. Methods of alignment of sequences for comparison are well-known in the art. Optimal alignment of sequences for comparison can be conducted, e.g., by the local homology algorithm of Smith & Waterman, *Adv. Appl. Math.* 2:482 (1981), by the homology alignment algorithm of Needleman & Wunsch, *J. Mol. Biol.* 48:443 (1970), by the search for similarity method of Pearson & Lipman, *Proc. Nat'l. Acad. Sci. USA* 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, WI), or by manual alignment and visual inspection (*see, e.g., Current Protocols in Molecular Biology* (Ausubel *et al.*, eds. 1995 supplement)).

[57] Preferred examples of algorithms that are suitable for determining percent sequence identity and sequence similarity include the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al., Nuc. Acids Res.* 25:3389-3402 (1977) and Altschul *et al., J. Mol. Biol.* 215:403-410 (1990). BLAST and BLAST 2.0 are used, with the parameters described herein, to determine percent sequence identity for the nucleic acids and proteins of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/).

This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al., supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, e.g., for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, M=5, N=-4 and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (*see* Henikoff & Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915 (1989)) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a comparison of both strands.

[58] The BLAST algorithm also performs a statistical analysis of the similarity between two sequences (*see, e.g.,* Karlin & Altschul, *Proc. Nat'l. Acad. Sci. USA* 90:5873-5787 (1993)). One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a nucleic acid is considered similar to a reference sequence if the smallest sum probability in a comparison of the test nucleic acid to the reference nucleic acid is less than about 0.2, more preferably less than about 0.01, and most preferably less than about 0.001. Log values may be large negative numbers, e.g., 5, 10, 20, 30, 40, 40, 70, 90, 110, 150, 170, etc.

[59] In one embodiment, the nucleic acid homology is determined through hybridization studies. Thus, for example, nucleic acids which hybridize under high stringency to the nucleic acid sequences which encode the peptides identified in Table 1 or Table 2, or their complements, are considered a colorectal cancer sequence. High stringency

conditions are known in the art; see for example Maniatis et al., Molecular Cloning: A Laboratory Manual, 2d Edition, 1989, and Short Protocols in Molecular Biology, ed. Ausubel, et al., both of which are hereby incorporated by reference. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures. An extensive guide to the hybridization of nucleic acids is found in Tijssen, Techniques in Biochemistry and Molecular Biology--Hybridization with Nucleic Acid Probes, "Overview of principles of hybridization and the strategy of nucleic acid assays" (1993). Generally, stringent conditions are selected to be about 5-10°C lower than the thermal melting point (Tm) for the specific sequence at a defined ionic strength pH. The Tm is the temperature (under defined ionic strength, pH and nucleic acid concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at Tm, 50% of the probes are occupied at equilibrium). Stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes (e.g. 10 to 50 nucleotides) and at least about 60°C for long probes (e.g. greater than 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide.

[60] In another embodiment, less stringent hybridization conditions are used; for example, moderate or low stringency conditions may be used, as are known in the art; see Maniatis and Ausubel, supra, and Tijssen, supra. For selective or specific hybridization, a positive signal is at least two times background, preferably 10 times background hybridization. Exemplary stringent hybridization conditions can be as following: 50% formamide, 5x SSC, and 1% SDS, incubating at 42°C, or, 5x SSC, 1% SDS, incubating at 65°C, with wash in 0.2x SSC, and 0.1% SDS at 65°C.

[61] Nucleic acids that do not hybridize to each other under stringent conditions are still substantially identical if the polypeptides which they encode are substantially identical. This occurs, for example, when a copy of a nucleic acid is created using the maximum codon degeneracy permitted by the genetic code. In such cases, the nucleic acids typically hybridize under moderately stringent hybridization conditions. Exemplary "moderately stringent hybridization conditions" include a hybridization in a buffer of 40% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 1X SSC at 45°C. A positive hybridization is at least twice background. Those of ordinary skill will readily

recognize that alternative hybridization and wash conditions can be utilized to provide conditions of similar stringency. Additional guidelines for determining hybridization parameters are provided in numerous reference, e.g., and *Current Protocols in Molecular Biology*, ed. Ausubel, *et al.*

[62] For PCR, a temperature of about 36°C is typical for low stringency amplification, although annealing temperatures may vary between about 32°C and 48°C depending on primer length. For high stringency PCR amplification, a temperature of about 62°C is typical, although high stringency annealing temperatures can range from about 50°C to about 65°C, depending on the primer length and specificity. Typical cycle conditions for both high and low stringency amplifications include a denaturation phase of 90°C - 95°C for 30 sec - 2 min., an annealing phase lasting 30 sec. - 2 min., and an extension phase of about 72°C for 1 - 2 min. Protocols and guidelines for low and high stringency amplification reactions are provided, e.g., in Innis *et al.*, *PCR Protocols, A Guide to Methods and Applications* (1990).

[63] In addition, the colorectal cancer nucleic acid sequences of the invention are fragments of larger genes, i.e. they are nucleic acid segments. "Genes" in this context includes coding regions, non-coding regions, and mixtures of coding and non-coding regions. Accordingly, as will be appreciated by those in the art, using the sequences provided herein, additional sequences of the colorectal cancer genes can be obtained, using techniques well known in the art for cloning either longer sequences or the full length sequences; see Maniatis et al., and Ausubel, et al., supra, hereby expressly incorporated by reference.

[64] An indication that two nucleic acid sequences or polypeptides are substantially identical is that the polypeptide encoded by the first nucleic acid is immunologically cross reactive with the antibodies raised against the polypeptide encoded by the second nucleic acid. Thus, a polypeptide is typically substantially identical to a second polypeptide, e.g., where the two peptides differ only by conservative substitutions. Another indication that two nucleic acid sequences are substantially identical is that the two molecules or their complements hybridize to each other under stringent conditions, as described above. Yet another indication that two nucleic acid sequences are substantially identical is that the same primers can be used to amplify the sequences.

[65] Once the colorectal cancer nucleic acid is identified, it can be cloned and, if necessary, its constituent parts recombined to form the entire colorectal cancer nucleic acid. Once isolated from its natural source, e.g., contained within a plasmid or other vector

or excised therefrom as a linear nucleic acid segment, the recombinant colorectal cancer nucleic acid can be further-used as a probe to identify and isolate other colorectal cancer nucleic acids, for example additional coding regions. It can also be used as a "precursor" nucleic acid to make modified or variant colorectal cancer nucleic acids and proteins.

[66] The colorectal cancer nucleic acids of the present invention are used in several ways. In a first embodiment, nucleic acid probes to the colorectal cancer nucleic acids are made and attached to biochips to be used in screening and diagnostic methods, as outlined below, or for administration, for example for gene therapy and/or antisense applications. Alternatively, the colorectal cancer nucleic acids that include coding regions of colorectal cancer proteins can be put into expression vectors for the expression of colorectal cancer proteins, again either for screening purposes or for administration to a patient.

[67] In a preferred embodiment, nucleic acid probes to colorectal cancer nucleic acids (both the nucleic acid sequences encoding peptides outlined in the Table 1 or Table 2 and/or the complements thereof) are made. The nucleic acid probes attached to the biochip are designed to be substantially complementary to the colorectal cancer nucleic acids, i.e. the target sequence (either the target sequence of the sample or to other probe sequences, for example in sandwich assays), such that hybridization of the target sequence and the probes of the present invention occurs. As outlined below, this complementarity need not be perfect; there may be any number of base pair mismatches which will interfere with hybridization between the target sequence and the single stranded nucleic acids of the present invention. However, if the number of mutations is so great that no hybridization can occur under even the least stringent of hybridization conditions, the sequence is not a complementary target sequence. Thus, by "substantially complementary" herein is meant that the probes are sufficiently complementary to the target sequences to hybridize under normal reaction conditions, particularly high stringency conditions, as outlined herein.

[68] A nucleic acid probe is generally single stranded but can be partially single and partially double stranded. The strandedness of the probe is dictated by the structure, composition, and properties of the target sequence. In general, the nucleic acid probes range from about 8 to about 100 bases long, with from about 10 to about 80 bases being preferred, and from about 30 to about 50 bases being particularly preferred. That is, generally whole genes are not used. In some embodiments, much longer nucleic acids can be used, up to hundreds of bases.

[69] In a preferred embodiment, more than one probe per sequence is used, with either overlapping probes or probes to different sections of the target being used. That

is, two, three, four or more probes, with three being preferred, are used to build in a redundancy for a particular target. The probes can be overlapping (i.e. have some sequence in common), or separate.

[70] As will be appreciated by those in the art, nucleic acids can be attached or immobilized to a solid support in a wide variety of ways. By "immobilized" and grammatical equivalents herein is meant the association or binding between the nucleic acid probe and the solid support is sufficient to be stable under the conditions of binding, washing, analysis, and removal as outlined below. The binding can be covalent or non-covalent. By "non-covalent binding" and grammatical equivalents herein is meant one or more of either electrostatic, hydrophilic, and hydrophobic interactions. Included in non-covalent binding is the covalent attachment of a molecule, such as, streptavidin to the support and the non-covalent binding of the biotinylated probe to the streptavidin. By "covalent binding" and grammatical equivalents herein is meant that the two moieties, the solid support and the probe, are attached by at least one bond, including sigma bonds, pi bonds and coordination bonds. Covalent bonds can be formed directly between the probe and the solid support or can be formed by a cross linker or by inclusion of a specific reactive group on either the solid support or the probe or both molecules. Immobilization may also involve a combination of covalent and non-covalent interactions.

[71] In general, the probes are attached to the biochip in a wide variety of ways, as will be appreciated by those in the art. As described herein, the nucleic acids can either be synthesized first, with subsequent attachment to the biochip, or can be directly synthesized on the biochip.

[72] The biochip comprises a suitable solid substrate. By "substrate" or "solid support" or other grammatical equivalents herein is meant any material that can be modified to contain discrete individual sites appropriate for the attachment or association of the nucleic acid probes and is amenable to at least one detection method. As will be appreciated by those in the art, the number of possible substrates are very large, and include, but are not limited to, glass and modified or functionalized glass, plastics (including acrylics, polystyrene and copolymers of styrene and other materials, polypropylene, polyethylene, polybutylene, polyurethanes, TeflonJ, etc.), polysaccharides, nylon or nitrocellulose, resins, silica or silica-based materials including silicon and modified silicon, carbon, metals, inorganic glasses, plastics, etc. In general, the substrates allow optical detection and do not appreciably fluoresce. A preferred substrate is described in copending application entitled

Reusable Low Fluorescent Plastic Biochip, U.S. Application Serial No. 09/270,214, filed March 15, 1999, herein incorporated by reference in its entirety.

[73] Generally the substrate is planar, although as will be appreciated by those in the art, other configurations of substrates may be used as well. For example, the probes may be placed on the inside surface of a tube, for flow-through sample analysis to minimize sample volume. Similarly, the substrate may be flexible, such as a flexible foam, including closed cell foams made of particular plastics.

[74] In a preferred embodiment, the surface of the biochip and the probe may be derivatized with chemical functional groups for subsequent attachment of the two. Thus, for example, the biochip is derivatized with a chemical functional group including, but not limited to, amino groups, carboxy groups, oxo groups and thiol groups, with amino groups being particularly preferred. Using these functional groups, the probes can be attached using functional groups on the probes. For example, nucleic acids containing amino groups can be attached to surfaces comprising amino groups, for example using linkers as are known in the art; for example, homo-or hetero-bifunctional linkers as are well known (see 1994 Pierce Chemical Company catalog, technical section on cross-linkers, pages 155-200, incorporated herein by reference). In addition, in some cases, additional linkers, such as alkyl groups (including substituted and heteroalkyl groups) may be used.

[75] In this embodiment, the oligonucleotides are synthesized as is known in the art, and then attached to the surface of the solid support. As will be appreciated by those skilled in the art, either the 5' or 3' terminus may be attached to the solid support, or attachment may be via an internal nucleoside.

[76] In an additional embodiment, the immobilization to the solid support may be very strong, yet non-covalent. For example, biotinylated oligonucleotides can be made, which bind to surfaces covalently coated with streptavidin, resulting in attachment.

[77] Alternatively, the oligonucleotides may be synthesized on the surface, as is known in the art. For example, photoactivation techniques utilizing photopolymerization compounds and techniques are used. In a preferred embodiment, the nucleic acids can be synthesized in situ, using well known photolithographic techniques, such as those described in WO 95/25116; WO 95/35505; U.S. Patent Nos. 5,700,637 and 5,445,934; and references cited within, all of which are expressly incorporated by reference; these methods of attachment form the basis of the Affimetrix GeneChip™ technology.

[78] In a preferred embodiment, colorectal cancer nucleic acids encoding colorectal cancer proteins are used to make a variety of expression vectors to express colorectal cancer proteins which can then be used in screening assays, as described below. The expression vectors may be either self-replicating extrachromosomal vectors or vectors which integrate into a host genome. Generally, these expression vectors include transcriptional and translational regulatory nucleic acid operably linked to the nucleic acid encoding the colorectal cancer protein. The term "control sequences" refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. The control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

[79] Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice. The transcriptional and translational regulatory nucleic acid will generally be appropriate to the host cell used to express the colorectal cancer protein; for example, transcriptional and translational regulatory nucleic acid sequences from Bacillus are preferably used to express the colorectal cancer protein in Bacillus. Numerous types of appropriate expression vectors, and suitable regulatory sequences are known in the art for a variety of host cells.

[80] In general, the transcriptional and translational regulatory sequences may include, but are not limited to, promoter sequences, ribosomal binding sites, transcriptional start and stop sequences, translational start and stop sequences, and enhancer or activator sequences. In a preferred embodiment, the regulatory sequences include a promoter and transcriptional start and stop sequences.

[81] Promoter sequences encode either constitutive or inducible promoters. The promoters may be either naturally occurring promoters or hybrid promoters. Hybrid

promoters, which combine elements of more than one promoter, are also known in the art, and are useful in the present invention.

[82] In addition, the expression vector may comprise additional elements. For example, the expression vector may have two replication systems, thus allowing it to be maintained in two organisms, for example in mammalian or insect cells for expression and in a procaryotic host for cloning and amplification. Furthermore, for integrating expression vectors, the expression vector contains at least one sequence homologous to the host cell genome, and preferably two homologous sequences which flank the expression construct. The integrating vector may be directed to a specific locus in the host cell by selecting the appropriate homologous sequence for inclusion in the vector. Constructs for integrating vectors are well known in the art.

[83] In addition, in a preferred embodiment, the expression vector contains a selectable marker gene to allow the selection of transformed host cells. Selection genes are well known in the art and will vary with the host cell used.

[84] The colorectal cancer proteins of the present invention are produced by culturing a host cell transformed with an expression vector containing nucleic acid encoding a colorectal cancer protein, under the appropriate conditions to induce or cause expression of the colorectal cancer protein. The conditions appropriate for colorectal cancer protein expression will vary with the choice of the expression vector and the host cell, and will be easily ascertained by one skilled in the art through routine experimentation. For example, the use of constitutive promoters in the expression vector will require optimizing the growth and proliferation of the host cell, while the use of an inducible promoter requires the appropriate growth conditions for induction. In addition, in some embodiments, the timing of the harvest is important. For example, the baculoviral systems used in insect cell expression are lytic viruses, and thus harvest time selection can be crucial for product yield.

[85] Appropriate host cells include yeast, bacteria, archaebacteria, fungi, and insect and animal cells, including mammalian cells. Of particular interest are Drosophila melangaster cells, Saccharomyces cerevisiae and other yeasts, E. coli, Bacillus subtilis, Sf9 cells, C129 cells, 293 cells, Neurospora, BHK, CHO, COS, HeLa cells, THP1 cell line (a macrophage cell line) and human cells and cell lines.

[86] In a preferred embodiment, the colorectal cancer proteins are expressed in mammalian cells. Mammalian expression systems are also known in the art, and include retroviral systems. A preferred expression vector system is a retroviral vector system such as is generally described in PCT/US97/01019 and PCT/US97/01048, both of which are

hereby expressly incorporated by reference. Of particular use as mammalian promoters are the promoters from mammalian viral genes, since the viral genes are often highly expressed and have a broad host range. Examples include the SV40 early promoter, mouse mammary tumor virus LTR promoter, adenovirus major late promoter, herpes simplex virus promoter, and the CMV promoter. Typically, transcription termination and polyadenylation sequences recognized by mammalian cells are regulatory regions located 3' to the translation stop codon and thus, together with the promoter elements, flank the coding sequence. Examples of transcription terminator and polyadenlytion signals include those derived form SV40.

[87] The methods of introducing exogenous nucleic acid into mammalian hosts, as well as other hosts, is well known in the art, and will vary with the host cell used. Techniques include dextran-mediated transfection, calcium phosphate precipitation, polybrene mediated transfection, protoplast fusion, electroporation, viral infection, encapsulation of the polynucleotide(s) in liposomes, and direct microinjection of the DNA into nuclei.

[88] In a preferred embodiment, colorectal cancer proteins are expressed in bacterial systems. Bacterial expression systems are well known in the art. Promoters from bacteriophage may also be used and are known in the art. In addition, synthetic promoters and hybrid promoters are also useful; for example, the tac promoter is a hybrid of the trp and lac promoter sequences. Furthermore, a bacterial promoter can include naturally occurring promoters of non-bacterial origin that have the ability to bind bacterial RNA polymerase and initiate transcription. In addition to a functioning promoter sequence, an efficient ribosome binding site is desirable. The expression vector may also include a signal peptide sequence that provides for secretion of the colorectal cancer protein in bacteria. The protein is either secreted into the growth media (gram-positive bacteria) or into the periplasmic space, located between the inner and outer membrane of the cell (gram-negative bacteria). The bacterial expression vector may also include a selectable marker gene to allow for the selection of bacterial strains that have been transformed. Suitable selection genes include genes which render the bacteria resistant to drugs such as ampicillin, chloramphenicol, erythromycin, kanamycin, neomycin and tetracycline. Selectable markers also include biosynthetic genes, such as those in the histidine, tryptophan and leucine biosynthetic pathways. These components are assembled into expression vectors. Expression vectors for bacteria are well known in the art, and include vectors for Bacillus subtilis, E. coli, Streptococcus cremoris, and Streptococcus lividans, among others. The bacterial expression vectors are transformed

into bacterial host cells using techniques well known in the art, such as calcium chloride treatment, electroporation, and others.

[89] In one embodiment, colorectal cancer proteins are produced in insect cells. Expression vectors for the transformation of insect cells, and in particular, baculovirus-based expression vectors, are well known in the art.

[90] In a preferred embodiment, colorectal cancer protein is produced in yeast cells. Yeast expression systems are well known in the art, and include expression vectors for Saccharomyces cerevisiae, Candida albicans and C. maltosa, Hansenula polymorpha, Kluyveromyces fragilis and K. lactis, Pichia guillerimondii and P. pastoris, Schizosaccharomyces pombe, and Yarrowia lipolytica.

[91] The colorectal cancer protein may also be made as a fusion protein, using techniques well known in the art. Thus, for example, for the creation of monoclonal antibodies, if the desired epitope is small, the colorectal cancer protein may be fused to a carrier protein to form an immunogen. Alternatively, the colorectal cancer protein may be made as a fusion protein to increase expression, or for other reasons. For example, when the colorectal cancer protein is a colorectal cancer peptide, the nucleic acid encoding the peptide may be linked to other nucleic acid for expression purposes.

[92] In one embodiment, the colorectal cancer nucleic acids, proteins and antibodies of the invention are labeled. By "labeled" herein is meant that a compound has at least one element, isotope or chemical compound attached to enable the detection of the compound. In general, labels fall into three classes: a) isotopic labels, which may be radioactive or heavy isotopes; b) immune labels, which may be antibodies or antigens; and c) colored or fluorescent dyes. The labels may be incorporated into the colorectal cancer nucleic acids, proteins and antibodies at any position. For example, the label should be capable of producing, either directly or indirectly, a detectable signal. The detectable moiety may be a radioisotope, such as 3H, 14C, 32P, 35S, or 125I, a fluorescent or chemiluminescent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactosidase or horseradish peroxidase. Any method known in the art for conjugating the antibody to the label may be employed, including those methods described by Hunter et al., Nature, 144:945 (1962); David et al., Biochemistry, 13:1014 (1974); Pain et al., J. Immunol. Meth., 40:219 (1981); and Nygren, J. Histochem. and Cytochem., 30:407 (1982).

[93] Accordingly, the present invention also provides colorectal cancer protein sequences. A colorectal cancer protein of the present invention may be identified in

several ways. "Protein" in this sense includes proteins, polypeptides, and peptides terms which are used interchangeably herein to refer to a polymer of amino acid residues. The terms apply to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers, those containing modified residues, and non-naturally occurring amino acid polymer.

[94] As will be appreciated by those in the art, the nucleic acid sequences of the invention can be used to generate protein sequences. There are a variety of ways to do this, including cloning the entire gene and verifying its frame and amino acid sequence, or by comparing it to known sequences to search for homology to provide a frame, assuming the colorectal cancer protein has homology to some protein in the database being used. Generally, the nucleic acid sequences are input into a program that will search all three frames for homology. This is done in a preferred embodiment using the following NCBI Advanced BLAST parameters. The program is blastx or blastn. The database is nr. The input data is as "Sequence in FASTA format". The organism list is "none". The "expect" is 10; the filter is default. The "descriptions" is 500, the "alignments" is 500, and the "alignment view" is pairwise. The "Query Genetic Codes" is standard (1). The matrix is BLOSUM62; gap existence cost is 11, per residue gap cost is 1; and the lambda ratio is .85 default. This results in the generation of a putative protein sequence.

[95] Also included within one embodiment of colorectal cancer proteins are amino acid variants of the naturally occurring sequences, as determined herein. Preferably, the variants are preferably greater than about 75% homologous to the wild-type sequence, more preferably greater than about 80%, even more preferably greater than about 85% and most preferably greater than 90%. In some embodiments the homology will be as high as about 93 to 95 or 98%. As for nucleic acids, homology in this context means sequence similarity or identity, with identity being preferred. This homology will be determined using standard techniques known in the art as are outlined above for the nucleic acid homologies.

[96] Colorectal cancer proteins of the present invention may be shorter or longer than the wild type amino acid sequences. Thus, in a preferred embodiment, included within the definition of colorectal cancer proteins are portions or fragments of the wild type sequences. herein. In addition, as outlined above, the colorectal cancer nucleic acids of the invention may be used to obtain additional coding regions, and thus additional protein sequence, using techniques known in the art.

[97] In a preferred embodiment, the colorectal cancer proteins are derivative or variant colorectal cancer proteins as compared to the wild-type sequence. That is, as outlined more fully below, the derivative colorectal cancer peptide will contain at least one amino acid substitution, deletion or insertion, with amino acid substitutions being particularly preferred. The amino acid substitution, insertion or deletion may occur at any residue within the colorectal cancer peptide.

[98] Also included in an embodiment of colorectal cancer proteins of the present invention are amino acid sequence variants. These variants fall into one or more of three classes: substitutional, insertional or deletional variants. These variants ordinarily are prepared by site specific mutagenesis of nucleotides in the DNA encoding the colorectal cancer protein, using cassette or PCR mutagenesis or other techniques well known in the art, to produce DNA encoding the variant, and thereafter expressing the DNA in recombinant cell culture as outlined above. However, variant colorectal cancer protein fragments having up to about 100-150 residues may be prepared by in vitro synthesis using established techniques. Amino acid sequence variants are characterized by the predetermined nature of the variation, a feature that sets them apart from naturally occurring allelic or interspecies variation of the colorectal cancer protein amino acid sequence. The variants typically exhibit the same qualitative biological activity as the naturally occurring analogue, although variants can also be selected which have modified characteristics as will be more fully outlined below.

[99] While the site or region for introducing an amino acid sequence variation is predetermined, the mutation per se need not be predetermined. For example, in order to optimize the performance of a mutation at a given site, random mutagenesis may be conducted at the target codon or region and the expressed colorectal cancer variants screened for the optimal combination of desired activity. Techniques for making substitution mutations at predetermined sites in DNA having a known sequence are well known, for example, M13 primer mutagenesis and PCR mutagenesis. Screening of the mutants is done using assays of colorectal cancer protein activities.

[100] Amino acid substitutions are typically of single residues; insertions usually will be on the order of from about 1 to 20 amino acids, although considerably larger insertions may be tolerated. Deletions range from about 1 to about 20 residues, although in some cases deletions may be much larger.

[101] Substitutions, deletions, insertions or any combination thereof may be used to arrive at a final derivative. Generally these changes are done on a few amino acids to minimize the alteration of the molecule. However, larger changes may be tolerated in certain

circumstances. When small alterations in the characteristics of the colorectal cancer protein are desired, substitutions are generally made in accordance with the following chart:

Chart I

Original Residue	Exemplary Substitutions
Ala	Ser
Arg	Lys
Asn	Gln, His
Asp	Glu
Cys	Ser
Gln	Asn
Glu	Asp
Gly	Pro
His	Asn, Gln
Ile	Leu, Val
Leu	Ile, Val
Lys	Arg, Gln, Glu
Met	Leu, Ile
Phe	Met, Leu, Tyr
Ser	Thr
Thr	Ser
Trp	Tyr
Tyr	Trp, Phe
Val	Ile, Leu

[102] Substantial changes in function or immunological identity are made by selecting substitutions that are less conservative than those shown in Chart I. For example, substitutions may be made which more significantly affect: the structure of the polypeptide backbone in the area of the alteration, for example the alpha-helical or beta-sheet structure; the charge or hydrophobicity of the molecule at the target site; or the bulk of the side chain. The substitutions which in general are expected to produce the greatest changes in the polypeptide's properties are those in which (a) a hydrophilic residue, e.g. seryl or threonyl is substituted for (or by) a hydrophobic residue, e.g. leucyl, isoleucyl, phenylalanyl, valyl or alanyl; (b) a cysteine or proline is substituted for (or by) any other residue; (c) a residue

having an electropositive side chain, e.g. lysyl, arginyl, or histidyl, is substituted for (or by) an electronegative residue, e.g. glutamyl or aspartyl; or (d) a residue having a bulky side chain, e.g. phenylalanine, is substituted for (or by) one not having a side chain, e.g. glycine.

[103] The variants typically exhibit the same qualitative biological activity and will elicit the same immune response as the naturally-occurring analogue, although variants also are selected to modify the characteristics of the colorectal cancer proteins as needed. Alternatively, the variant may be designed such that the biological activity of the colorectal cancer protein is altered. For example, glycosylation sites may be altered or removed.

[104] Covalent modifications of colorectal cancer polypeptides are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a colorectal cancer polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N-or C-terminal residues of a colorectal cancer polypeptide. Derivatization with bifunctional agents is useful, for instance, for crosslinking colorectal cancer to a water-insoluble support matrix or surface for use in the method for purifying anti-colorectal cancer antibodies or screening assays, as is more fully described below. Commonly used crosslinking agents include, e.g., 1,1-bis(diazo-acetyl)-2-phenylethane, glutaraldehyde, N-hydroxy-succinimide esters, for example, esters with 4-azido-salicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis-(succinimidyl-propionate), bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-[(p-azidophenyl)-dithio]pro-pioimi-date.

[105] Other modifications include deamidation of glutaminyl and asparaginyl residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl, threonyl or tyrosyl residues, methylation of the α-amino groups of lysine, arginine, and histidine side chains [T.E. Creighton, Proteins: Structure and Molecular Properties, W.H. Freeman & Co., San Francisco, pp. 79-86 (1983)], acetylation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

[106] Another type of covalent modification of the colorectal cancer polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence colorectal cancer polypeptide, and/or adding one or more glycosylation sites that are not present in the native sequence colorectal cancer polypeptide.

[107] Addition of glycosylation sites to colorectal cancer polypeptides may be accomplished by altering the amino acid sequence thereof. The alteration may be made, for example, by the addition of, or substitution by, one or more serine or threonine residues to the native sequence colorectal cancer polypeptide (for O-linked glycosylation sites). The colorectal cancer amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the colorectal cancer polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

[108] Another means of increasing the number of carbohydrate moieties on the colorectal cancer polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330 published 11 September 1987, and in Aplin and Wriston, colorectal cancer Crit. Rev. Biochem., pp. 259-306 (1981).

[109] Removal of carbohydrate moieties present on the colorectal cancer polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, for instance, by Hakimuddin, et al., Arch. Biochem. Biophys., 259:52 (1987) and by Edge et al., Anal. Biochem., 118:131 (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety of endo-and exo-glycosidases as described by Thotakura et al., Meth. Enzymol., 138:350 (1987).

[110] Another type of covalent modification of colorectal cancer comprises linking the colorectal cancer polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol, polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337.

[111] colorectal cancer polypeptides of the present invention may also be modified in a way to form chimeric molecules comprising a colorectal cancer polypeptide fused to another, heterologous polypeptide or amino acid sequence. In one embodiment, such a chimeric molecule comprises a fusion of a colorectal cancer polypeptide with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino-or carboxyl-terminus of the colorectal cancer polypeptide. The presence of such epitope-tagged forms of a colorectal cancer polypeptide can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the colorectal cancer polypeptide to be readily purified by affinity purification

using an anti-tag antibody or another type of affinity matrix that binds to the epitope tag. In an alternative embodiment, the chimeric molecule may comprise a fusion of a colorectal cancer polypeptide with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule, such a fusion could be to the Fc region of an IgG molecule.

[112] Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; the flu HA tag polypeptide and its antibody 12CA5 [Field et al., Mol. Cell. Biol., 8:2159-2165 (1988)]; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7 and 9E10 antibodies thereto [Evan et al., Molecular and Cellular Biology, 5:3610-3616 (1985)]; and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody [Paborsky et al., Protein Engineering, 3(6):547-553 (1990)]. Other tag polypeptides include the Flag-peptide [Hopp et al., BioTechnology, 6:1204-1210 (1988)]; the KT3 epitope peptide [Martin et al., Science, 255:192-194 (1992)]; tubulin epitope peptide [Skinner et al., J. Biol. Chem., 266:15163-15166 (1991)]; and the T7 gene 10 protein peptide tag [Lutz-Freyermuth et al., Proc. Natl. Acad. Sci. USA, 87:6393-6397 (1990)].

[113] Also included with the definition of colorectal cancer protein in one embodiment are other colorectal cancer proteins of the colorectal cancer family, and colorectal cancer proteins from other organisms, which are cloned and expressed as outlined below. Thus, probe or degenerate polymerase chain reaction (PCR) primer sequences may be used to find other related colorectal cancer proteins from humans or other organisms. As will be appreciated by those in the art, particularly useful probe and/or PCR primer sequences include the unique areas of the colorectal cancer nucleic acid sequence. As is generally known in the art, preferred PCR primers are from about 15 to about 35 nucleotides in length, with from about 20 to about 30 being preferred, and may contain inosine as needed. The conditions for the PCR reaction are well known in the art.

[114] In addition, as is outlined herein, colorectal cancer proteins can be made that are longer than those depicted in the Table 1 or Table 2 for example, by the elucidation of additional sequences, the addition of epitope or purification tags, the addition of other fusion sequences, etc.

[115] Colorectal cancer proteins may also be identified as being encoded by colorectal cancer nucleic acids. Thus, colorectal cancer proteins are encoded by nucleic acids that will hybridize to the sequences of the sequence listings, or their complements, as outlined herein.

[116] In a preferred embodiment, when the colorectal cancer protein is to be used to generate antibodies, for example for immunotherapy, the colorectal cancer protein should share at least one epitope or determinant with the full length protein. By "epitope" or "determinant" herein is meant a portion of a protein which will generate and/or bind an antibody or T-cell receptor in the context of MHC. Thus, in most instances, antibodies made to a smaller colorectal cancer protein will be able to bind to the full length protein. In a preferred embodiment, the epitope is unique; that is, antibodies generated to a unique epitope show little or no cross-reactivity. In a preferred embodiment, the epitope is selected from a peptide encoded by a nucleic acid of Table1. In another preferred embodiment, the epitope is selected from the CBF9 peptide sequence shown in Table 2.

[117] In one embodiment, the term “antibody” includes antibody fragments, as are known in the art, including Fab, Fab2, single chain antibodies (Fv for example), chimeric antibodies, etc., either produced by the modification of whole antibodies or those synthesized de novo using recombinant DNA technologies.

[118] Methods of preparing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include the CBF9 peptide of Table 2, or a peptide encoded by a nucleic acid of Table 1 or fragment thereof or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

[119] The antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein, Nature, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized in vitro. The immunizing agent will typically include the CBF9 polypeptide or a peptide encoded by a

nucleic acid of Table 1 or a fragment thereof or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell [Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103]. Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

[120] In one embodiment, the antibodies are bispecific antibodies. Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for a colorectal cancer protein or a fragment thereof, the other one is for any other antigen, and preferably for a cell-surface protein or receptor or receptor subunit, preferably one that is tumor specific.

[121] In a preferred embodiment, the antibodies to colorectal cancer are capable of reducing or eliminating the biological function of colorectal cancer , as is described below. That is, the addition of anti-colorectal cancer antibodies (either polyclonal or preferably monoclonal) to colorectal cancer (or cells containing colorectal cancer) may reduce or eliminate the colorectal cancer activity. Generally, at least a 25% decrease in activity is preferred, with at least about 50% being particularly preferred and about a 95-100% decrease being especially preferred.

[122] In a preferred embodiment the antibodies to the colorectal cancer proteins are humanized antibodies. Humanized forms of non-human (e.g., murine) antibodies are chimeric molecules of immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')2 or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues form a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired

specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin [Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-329 (1988); and Presta, Curr. Op. Struct. Biol., 2:593-596 (1992)].

[123] Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as import residues, which are typically taken from an import variable domain. Humanization can be essentially performed following the method of Winter and co-workers [Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); Verhoeyen et al., Science, 239:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such humanized antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

[124] Human antibodies can also be produced using various techniques known in the art, including phage display libraries [Hoogenboom and Winter, J. Mol. Biol., 227:381 (1991); Marks et al., J. Mol. Biol., 222:581 (1991)]. The techniques of Cole et al. and Boerner et al. are also available for the preparation of human monoclonal antibodies (Cole et al., Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, p. 77 (1985) and Boerner et al., J. Immunol., 147(1):86-95 (1991)]. Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire.

This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks et al., Bio/Technology 10, 779-783 (1992); Lonberg et al., Nature 368 856-859 (1994); Morrison, Nature 368, 812-13 (1994); Fishwild et al., Nature Biotechnology 14, 845-51 (1996); Neuberger, Nature Biotechnology 14, 826 (1996); Lonberg and Huszar, Intern. Rev. Immunol. 13 65-93 (1995).

[125] By immunotherapy is meant treatment of colorectal cancer with an antibody raised against colorectal cancer proteins. As used herein, immunotherapy can be passive or active. Passive immunotherapy as defined herein is the passive transfer of antibody to a recipient (patient). Active immunization is the induction of antibody and/or T-cell responses in a recipient (patient). Induction of an immune response is the result of providing the recipient with an antigen to which antibodies are raised. As appreciated by one of ordinary skill in the art, the antigen may be provided by injecting a polypeptide against which antibodies are desired to be raised into a recipient, or contacting the recipient with a nucleic acid capable of expressing the antigen and under conditions for expression of the antigen.

[126] In a preferred embodiment the colorectal cancer proteins against which antibodies are raised are secreted proteins as described above. Without being bound by theory, antibodies used for treatment, bind and prevent the secreted protein from binding to its receptor, thereby inactivating the secreted colorectal cancer protein.

[127] In another preferred embodiment, the colorectal cancer protein to which antibodies are raised is a transmembrane protein. Without being bound by theory, antibodies used for treatment, bind the extracellular domain of the colorectal cancer protein and prevent it from binding to other proteins, such as circulating ligands or cell-associated molecules. The antibody may cause down-regulation of the transmembrane colorectal cancer protein. As will be appreciated by one of ordinary skill in the art, the antibody may be a competitive, non-competitive or uncompetitive inhibitor of protein binding to the extracellular domain of the colorectal cancer protein. The antibody is also an antagonist of the colorectal cancer protein. Further, the antibody prevents activation of the transmembrane colorectal cancer protein. In one aspect, when the antibody prevents the binding of other molecules to the colorectal cancer protein, the antibody prevents growth of the cell. The antibody also sensitizes the cell to cytotoxic agents, including, but not limited to TNF-α, TNF-β, IL-1, INF-γ and IL-2, or chemotherapeutic agents including 5FU, vinblastine,

actinomycin D, cisplatin, methotrexate, and the like. In some instances the antibody belongs to a sub-type that activates serum complement when complexed with the transmembrane protein thereby mediating cytotoxicity. Thus, colorectal cancer is treated by administering to a patient antibodies directed against the transmembrane colorectal cancer protein.

[128] In another preferred embodiment, the antibody is conjugated to a therapeutic moiety. In one aspect the therapeutic moiety is a small molecule that modulates the activity of the colorectal cancer protein. In another aspect the therapeutic moiety modulates the activity of molecules associated with or in close proximity to the colorectal cancer protein. The therapeutic moiety may inhibit enzymatic activity such as protease or protein kinase activity associated with colorectal cancer .

[129] In a preferred embodiment, the therapeutic moiety may also be a cytotoxic agent. In this method, targeting the cytotoxic agent to tumor tissue or cells, results in a reduction in the number of afflicted cells, thereby reducing symptoms associated with colorectal cancer . Cytotoxic agents are numerous and varied and include, but are not limited to, cytotoxic drugs or toxins or active fragments of such toxins. Suitable toxins and their corresponding fragments include diptheria A chain, exotoxin A chain, ricin A chain, abrin A chain, curcin, crotin, phenomycin, enomycin and the like. Cytotoxic agents also include radiochemicals made by conjugating radioisotopes to antibodies raised against colorectal cancer proteins, or binding of a radionuclide to a chelating agent that has been covalently attached to the antibody. Targeting the therapeutic moiety to transmembrane colorectal cancer proteins not only serves to increase the local concentration of therapeutic moiety in the colorectal cancer afflicted area, but also serves to reduce deleterious side effects that may be associated with the therapeutic moiety.

[130] In another preferred embodiment, the colorectal cancer protein against which the antibodies are raised is an intracellular protein. In this case, the antibody may be conjugated to a protein which facilitates entry into the cell. In one case, the antibody enters the cell by endocytosis. In another embodiment, a nucleic acid encoding the antibody is administered to the individual or cell. Moreover, wherein the colorectal cancer protein can be targeted within a cell, i.e., the nucleus, an antibody thereto contains a signal for that target localization, i.e., a nuclear localization signal.

[131] The colorectal cancer antibodies of the invention specifically bind to colorectal cancer proteins. By "specifically bind" herein is meant that the antibodies bind to the protein with a binding constant in the range of at least 10^{-4}- 10^{-6} M^{-1}, with a preferred range being 10^{-7} - 10^{-9} M^{-1}.

[132] In a preferred embodiment, the colorectal cancer protein is purified or isolated after expression. Colorectal cancer proteins may be isolated or purified in a variety of ways known to those skilled in the art depending on what other components are present in the sample. Standard purification methods include electrophoretic, molecular, immunological and chromatographic techniques, including ion exchange, hydrophobic, affinity, and reverse-phase HPLC chromatography, and chromatofocusing. For example, the colorectal cancer protein may be purified using a standard anti-colorectal cancer antibody column. Ultrafiltration and diafiltration techniques, in conjunction with protein concentration, are also useful. For general guidance in suitable purification techniques, see Scopes, R., Protein Purification, Springer-Verlag, NY (1982). The degree of purification necessary will vary depending on the use of the colorectal cancer protein. In some instances no purification will be necessary.

[133] Once expressed and purified if necessary, the colorectal cancer proteins and nucleic acids are useful in a number of applications.

[134] In one aspect, the expression levels of genes are determined for different cellular states in the colorectal cancer phenotype; that is, the expression levels of genes in normal colon tissue and in colorectal cancer tissue (and in some cases, for varying severities of colorectal cancer that relate to prognosis, as outlined below) are evaluated to provide expression profiles. An expression profile of a particular cell state or point of development is essentially a "fingerprint" of the state; while two states may have any particular gene similarly expressed, the evaluation of a number of genes simultaneously allows the generation of a gene expression profile that is unique to the state of the cell. By comparing expression profiles of cells in different states, information regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained. Then, diagnosis may be done or confirmed: does tissue from a particular patient have the gene expression profile of normal or colorectal cancer tissue.

[135] "Differential expression," or grammatical equivalents as used herein, refers to both qualitative as well as quantitative differences in the genes' temporal and/or cellular expression patterns within and among the cells. Thus, a differentially expressed gene can qualitatively have its expression altered, including an activation or inactivation, in, for example, normal versus colorectal cancer tissue. That is, genes may be turned on or turned off in a particular state, relative to another state. As is apparent to the skilled artisan, any comparison of two or more states can be made. Such a qualitatively regulated gene will exhibit an expression pattern within a state or cell type which is detectable by standard

techniques in one such state or cell type, but is not detectable in both. Alternatively, the determination is quantitative in that expression is increased or decreased; that is, the expression of the gene is either upregulated, resulting in an increased amount of transcript, or downregulated, resulting in a decreased amount of transcript. The degree to which expression differs need only be large enough to quantify via standard characterization techniques as outlined below, such as by use of Affymetrix GeneChip™ expression arrays, Lockhart, Nature Biotechnology, 14:1675-1680 (1996), hereby expressly incorporated by reference. Other techniques include, but are not limited to, quantitative reverse transcriptase PCR, Northern analysis and RNase protection. As outlined above, preferably the change in expression (i.e. upregulation or downregulation) is at least about 50%, more preferably at least about 100%, more preferably at least about 150%, more preferably, at least about 200%, with from 300 to at least 1000% being especially preferred.

[136] As will be appreciated by those in the art, this may be done by evaluation at either the gene transcript, or the protein level; that is, the amount of gene expression may be monitored using nucleic acid probes to the DNA or RNA equivalent of the gene transcript, and the quantification of gene expression levels, or, alternatively, the final gene product itself (protein) can be monitored, for example through the use of antibodies to the colorectal cancer protein and standard immunoassays (ELISAs,e tc.) or other techniques, including mass spectroscopy assays, 2D gel electrophoresis assays, etc. Thus, the proteins corresponding to colorectal cancer genes, i.e. those identified as being important in a colorectal cancer phenotype, can be evaluated in a colorectal cancer diagnostic test.

[137] In a preferred embodiment, gene expression monitoring is done and a number of genes, i.e. an expression profile, is monitored simultaneously, although multiple protein expression monitoring can be done as well. Similarly, these assays may be done on an individual basis as well.

[138] In this embodiment, the colorectal cancer nucleic acid probes are attached to biochips as outlined herein for the detection and quantification of colorectal cancer sequences in a particular cell. The assays are further described below in the example.

[139] In a preferred embodiment nucleic acids encoding the colorectal cancer protein are detected. Although DNA or RNA encoding the colorectal cancer protein may be detected, of particular interest are methods wherein the mRNA encoding a colorectal cancer protein is detected. The presence of mRNA in a sample is an indication that the colorectal cancer gene has been transcribed to form the mRNA, and suggests that the protein

is expressed. Probes to detect the mRNA can be any nucleotide/deoxynucleotide probe that is complementary to and base pairs with the mRNA and includes but is not limited to oligonucleotides, cDNA or RNA. Probes also should contain a detectable label, as defined herein. In one method the mRNA is detected after immobilizing the nucleic acid to be examined on a solid support such as nylon membranes and hybridizing the probe with the sample. Following washing to remove the non-specifically bound probe, the label is detected. In another method detection of the mRNA is performed in situ. In this method permeabilized cells or tissue samples are contacted with a detectably labeled nucleic acid probe for sufficient time to allow the probe to hybridize with the target mRNA. Following washing to remove the non-specifically bound probe, the label is detected. For example a digoxygenin labeled riboprobe (RNA probe) that is complementary to the mRNA encoding a colorectal cancer protein is detected by binding the digoxygenin with an anti-digoxygenin secondary antibody and developed with nitro blue tetrazolium and 5-bromo-4-chloro-3-indoyl phosphate.

[140] In a preferred embodiment, any of the three classes of proteins as described herein (secreted, transmembrane or intracellular proteins) are used in diagnostic assays. The colorectal cancer proteins, antibodies, nucleic acids, modified proteins and cells containing colorectal cancer sequences are used in diagnostic assays. This can be done on an individual gene or corresponding polypeptide level. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes and/or corresponding polypeptides.

[141] As described and defined herein, colorectal cancer proteins, including intracellular, transmembrane or secreted proteins, find use as markers of colorectal cancer. Detection of these proteins in putative colorectal cancer tissue or patients allows for a determination or diagnosis of colorectal cancer. Numerous methods known to those of ordinary skill in the art find use in detecting colorectal cancer. In one embodiment, antibodies are used to detect colorectal cancer proteins. A preferred method separates proteins from a sample or patient by electrophoresis on a gel (typically a denaturing and reducing protein gel, but may be any other type of gel including isoelectric focusing gels and the like). Following separation of proteins, the colorectal cancer protein is detected by immunoblotting with antibodies raised against the colorectal cancer protein. Methods of immunoblotting are well known to those of ordinary skill in the art.

[142] In another preferred method, antibodies to the colorectal cancer protein find use in in situ imaging techniques. In this method cells are contacted with from one to many antibodies to the colorectal cancer protein(s). Following washing to remove non-specific antibody binding, the presence of the antibody or antibodies is detected. In one embodiment the antibody is detected by incubating with a secondary antibody that contains a detectable label. In another method the primary antibody to the colorectal cancer protein(s) contains a detectable label. In another preferred embodiment each one of multiple primary antibodies contains a distinct and detectable label. This method finds particular use in simultaneous screening for a plurality of colorectal cancer proteins. As will be appreciated by one of ordinary skill in the art, numerous other histological imaging techniques are useful in the invention.

[143] In a preferred embodiment the label is detected in a fluorometer which has the ability to detect and distinguish emissions of different wavelengths. In addition, a fluorescence activated cell sorter (FACS) can be used in the method.

[144] In another preferred embodiment, antibodies find use in diagnosing colorectal cancer from blood samples. As previously described, certain colorectal cancer proteins are secreted/circulating molecules. Blood samples, therefore, are useful as samples to be probed or tested for the presence of secreted colorectal cancer proteins. Antibodies can be used to detect the colorectal cancer by any of the previously described immunoassay techniques including ELISA, immunoblotting (Western blotting), immunoprecipitation, BIACORE technology and the like, as will be appreciated by one of ordinary skill in the art.

[145] In a preferred embodiment, in situ hybridization of labeled colorectal cancer nucleic acid probes to tissue arrays is done. For example, arrays of tissue samples, including colorectal cancer tissue and/or normal tissue, are made. In situ hybridization as is known in the art can then be done.

[146] It is understood that when comparing the fingerprints between an individual and a standard, the skilled artisan can make a diagnosis as well as a prognosis. It is further understood that the genes which indicate the diagnosis may differ from those which indicate the prognosis.

[147] In a preferred embodiment, the colorectal cancer proteins, antibodies, nucleic acids, modified proteins and cells containing colorectal cancer sequences are used in prognosis assays. As above, gene expression profiles can be generated that correlate to colorectal cancer severity, in terms of long term prognosis. Again, this may be done on either a protein or gene level, with the use of genes being preferred. As above, the colorectal

cancer probes are attached to biochips for the detection and quantification of colorectal cancer sequences in a tissue or patient. The assays proceed as outlined for diagnosis.

[148] In a preferred embodiment, any of the three classes of proteins as described herein are used in drug screening assays. The colorectal cancer proteins, antibodies, nucleic acids, modified proteins and cells containing colorectal cancer sequences are used in drug screening assays or by evaluating the effect of drug candidates on a "gene expression profile" or expression profile of polypeptides. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes after treatment with a candidate agent, Zlokarnik, et al., Science 279, 84-8 (1998), Heid, 1996 #69.

[149] In a preferred embodiment, the colorectal cancer proteins, antibodies, nucleic acids, modified proteins and cells containing the native or modified colorectal cancer proteins are used in screening assays. That is, the present invention provides novel methods for screening for compositions which modulate the colorectal cancer phenotype. As above, this can be done on an individual gene level or by evaluating the effect of drug candidates on a "gene expression profile". In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes after treatment with a candidate agent, see Zlokarnik, supra. Having identified the differentially expressed genes herein, a variety of assays may be executed. In a preferred embodiment, assays may be run on an individual gene or protein level. That is, having identified a particular gene as up regulated in colorectal cancer, candidate bioactive agents may be screened to modulate this gene's response; preferably to down regulate the gene, although in some circumstances to up regulate the gene.

[150] The phrase "functional effects" in the context of assays for testing compounds that modulate activity of a colorectal cancer protein or colorectal cancer nucleic acid includes the determination of a parameter that is indirectly or directly under the influence of a colorectal cancer protein or nucleic acid, *e.g.*, a physical (direct), or phenotypic or chemical effect (indirect), such as the ability to increase or decrease cellular proliferation. It includes cell cycle arrest, the ability of cells to proliferate, and other characteristics of proliferating cells. "Functional effects" include *in vitro*, *in vivo*, and *ex vivo* activities.

[151] By "determining the functional effect" is meant assaying for a compound that increases or decreases a parameter that is indirectly or directly under the influence of a colorectal cancer protein or nucleic acid, *e.g.*, physical, phenotypic and chemical effects. Such functional effects can be measured by any means known to those

skilled in the art, *e.g.*, physical effects such as changes in spectroscopic characteristics (*e.g.*, fluorescence, absorbance, refractive index); hydrodynamic (*e.g.*, shape); chromatographic; or solubility properties for the protein; measuring ligand binding activity or binding assays, *e.g.* binding to antibodies; measuring changes in ligand binding activity; and chemical or phenotypic effects such as measuring inducible markers or transcriptional activation of the protein; measuring cellular proliferation; measuring cell surface marker expression; measurement of changes in protein levels for colorectal cancer-associated sequences; measurement of RNA stability; phosphorylation or dephosphorylation; signal transduction, e.g., receptor-ligand interactions, second messenger concentrations (e.g., cAMP, IP3, or intracellular Ca^{2+}); identification of downstream or reporter gene expression (CAT, luciferase, β-gal, GFP and the like), *e.g.*, via chemiluminescence, fluorescence, colorimetric reactions, antibody binding, and inducible markers.

[152] "Inhibitors", "activators", and "modulators" of colorectal cancer polynucleotide and polypeptide sequences are used to refer to activating, inhibitory, or modulating molecules identified using *in vitro* and *in vivo* assays of colorectal cancer polynucleotide and polypeptide sequences. Inhibitors are compounds that, *e.g.*, bind to, partially or totally block activity, decrease, prevent, delay activation, inactivate, desensitize, or down regulate the activity or expression of colorectal cancer proteins or nucleic acids, *e.g.*, antagonists. "Activators" are compounds that increase, open, activate, facilitate, enhance activation, sensitize, agonize, or up regulate colorectal cancer protein or nucleic acid activity. Inhibitors, activators, or modulators also include genetically modified versions of colorectal cancer proteins, *e.g.*, versions with altered activity, as well as naturally occurring and synthetic ligands, antagonists, agonists, antibodies, antisense molecules, peptides, ribozymes, small chemical molecules and the like. Such assays for inhibitors and activators include, *e.g.*, expressing colorectal cancer protein *in vitro*, in cells, or cell membranes, applying putative modulator compounds, and then determining the functional effects on activity, as described above.

[153] Samples or assays comprising colorectal cancer proteins or colorectal cancer nucleic acids that are treated with a potential activator, inhibitor, or modulator are compared to control samples without the inhibitor, activator, or modulator to examine the extent of inhibition. Control samples (untreated with inhibitors) are assigned a relative activity value of 100%. Inhibition of colorectal cancer is achieved when the activity value relative to the control is about 80%, preferably 50%, more preferably 25-0%. Activation of

colorectal cancer is achieved when the activity value relative to the control (untreated with activators) is 110%, more preferably 150%, more preferably 200-500% (i.e., two to five fold higher relative to the control), more preferably 1000-3000% higher.

[154] As will be appreciated by those in the art, this may be done by evaluation at either the gene or the protein level; that is, the amount of gene expression may be monitored using nucleic acid probes and the quantification of gene expression levels, or, alternatively, the gene product itself can be monitored, for example through the use of antibodies to the colorectal cancer protein and standard immunoassays.

[155] In a preferred embodiment, gene expression monitoring is done and a number of genes, i.e. an expression profile, is monitored simultaneously, although multiple protein expression monitoring can be done as well.

[156] In this embodiment, the colorectal cancer nucleic acid probes are attached to biochips as outlined herein for the detection and quantification of colorectal cancer sequences in a particular cell. The assays are further described below.

[157] Generally, in a preferred embodiment, a candidate bioactive agent is added to the cells prior to analysis. Moreover, screens are provided to identify a candidate bioactive agent which modulates colorectal cancer, modulates colorectal cancer proteins, binds to a colorectal cancer protein, or interferes between the binding of a colorectal cancer protein and an antibody.

[158] The term "candidate bioactive agent" or "test compound" or "drug candidate" or "modulator" or grammatical equivalents as used herein describes any molecule, either naturally occurring or synthetic, e.g., protein, oligopeptide (e.g., from about 5 to about 25 amino acids in length, preferably from about 10 to 20 or 12 to 18 amino acids in length, preferably 12, 15, or 18 amino acids in length), small organic molecule, polysaccharide, lipid, fatty acid, polynucleotide, oligonucleotide, etc., to be tested for the capacity to directly or indirectly modulate colorectal cancer sequences, including both nucleic acid and protein sequences. The test compound can be in the form of a library of test compounds, such as a combinatorial or randomized library that provides a sufficient range of diversity. Test compounds are optionally linked to a fusion partner, e.g., targeting compounds, rescue compounds, dimerization compounds, stabilizing compounds, addressable compounds, and other functional moieties. Conventionally, new chemical entities with useful properties are generated by identifying a test compound (called a "lead compound") with some desirable property or activity, e.g., inhibiting activity, creating variants of the lead compound, and

evaluating the property and activity of those variant compounds. Often, high throughput screening (HTS) methods are employed for such an analysis.

[159] In preferred embodiments, the bioactive agents modulate the expression profiles, or expression profile nucleic acids or proteins provided herein. In a particularly preferred embodiment, the candidate agent suppresses a colorectal cancer phenotype, for example to a normal colon tissue fingerprint. Similarly, the candidate agent preferably suppresses a severe colorectal cancer phenotype. Generally a plurality of assay mixtures are run in parallel with different agent concentrations to obtain a differential response to the various concentrations. Typically, one of these concentrations serves as a negative control, i.e., at zero concentration or below the level of detection.

[160] In one aspect, a candidate agent will neutralize the effect of a colorectal cancer protein. By "neutralize" is meant that activity of a protein is either inhibited or counter acted against so as to have substantially no effect on a cell.

[161] Candidate agents encompass numerous chemical classes, though typically they are organic molecules, preferably small organic compounds having a molecular weight of more than 100 and less than about 2,500 daltons. Preferred small molecules are less than 2000, or less than 1500 or less than 1000 or less than 500 D. Candidate agents comprise functional groups necessary for structural interaction with proteins, particularly hydrogen bonding, and typically include at least an amine, carbonyl, hydroxyl or carboxyl group, preferably at least two of the functional chemical groups. The candidate agents often comprise cyclical carbon or heterocyclic structures and/or aromatic or polyaromatic structures substituted with one or more of the above functional groups. Candidate agents are also found among biomolecules including peptides, saccharides, fatty acids, steroids, purines, pyrimidines, derivatives, structural analogs or combinations thereof. Particularly preferred are peptides.

[162] Candidate agents are obtained from a wide variety of sources including libraries of synthetic or natural compounds. For example, numerous means are available for random and directed synthesis of a wide variety of organic compounds and biomolecules, including expression of randomized oligonucleotides. Alternatively, libraries of natural compounds in the form of bacterial, fungal, plant and animal extracts are available or readily produced. Additionally, natural or synthetically produced libraries and compounds are readily modified through conventional chemical, physical and biochemical means. Known pharmacological agents may be subjected to directed or random chemical modifications, such as acylation, alkylation, esterification, amidification to produce structural analogs.

[163] In a preferred embodiment, the candidate bioactive agents are proteins. By "protein" herein is meant at least two covalently attached amino acids, which includes proteins, polypeptides, oligopeptides and peptides. The protein may be made up of naturally occurring amino acids and peptide bonds, or synthetic peptidomimetic structures. Thus "amino acid", or "peptide residue", as used herein means both naturally occurring and synthetic amino acids. For example, homo-phenylalanine, citrulline and noreleucine are considered amino acids for the purposes of the invention. "Amino acid" also includes imino acid residues such as proline and hydroxyproline. The side chains may be in either the (R) or the (S) configuration. In the preferred embodiment, the amino acids are in the (S) or L-configuration. If non-naturally occurring side chains are used, non-amino acid substituents may be used, for example to prevent or retard in vivo degradations.

[164] In a preferred embodiment, the candidate bioactive agents are naturally occurring proteins or fragments of naturally occurring proteins. Thus, for example, cellular extracts containing proteins, or random or directed digests of proteinaceous cellular extracts, may be used. In this way libraries of procaryotic and eucaryotic proteins may be made for screening in the methods of the invention. Particularly preferred in this embodiment are libraries of bacterial, fungal, viral, and mammalian proteins, with the latter being preferred, and human proteins being especially preferred.

[165] In a preferred embodiment, the candidate bioactive agents are peptides of from about 5 to about 30 amino acids, with from about 5 to about 20 amino acids being preferred, and from about 7 to about 15 being particularly preferred. The peptides may be digests of naturally occurring proteins as is outlined above, random peptides, or "biased" random peptides. By "randomized" or grammatical equivalents herein is meant that each nucleic acid and peptide consists of essentially random nucleotides and amino acids, respectively. Since generally these random peptides (or nucleic acids, discussed below) are chemically synthesized, they may incorporate any nucleotide or amino acid at any position. The synthetic process can be designed to generate randomized proteins or nucleic acids, to allow the formation of all or most of the possible combinations over the length of the sequence, thus forming a library of randomized candidate bioactive proteinaceous agents.

[166] In one embodiment, the library is fully randomized, with no sequence preferences or constants at any position. In a preferred embodiment, the library is biased. That is, some positions within the sequence are either held constant, or are selected from a limited number of possibilities. For example, in a preferred embodiment, the nucleotides or amino acid residues are randomized within a defined class, for example, of hydrophobic

amino acids, hydrophilic residues, sterically biased (either small or large) residues, towards the creation of nucleic acid binding domains, the creation of cysteines, for cross-linking, prolines for SH-3 domains, serines, threonines, tyrosines or histidines for phosphorylation sites, etc., or to purines, etc.

[167] In a preferred embodiment, the candidate bioactive agents are nucleic acids, as defined above.

[168] As described above generally for proteins, nucleic acid candidate bioactive agents may be naturally occurring nucleic acids, random nucleic acids, or "biased" random nucleic acids. For example, digests of procaryotic or eucaryotic genomes may be used as is outlined above for proteins.

[169] In a preferred embodiment, the candidate bioactive agents are organic chemical moieties, a wide variety of which are available in the literature.

[170] "Antibody" refers to a polypeptide comprising a framework region from an immunoglobulin gene or fragments thereof that specifically binds and recognizes an antigen. The recognized immunoglobulin genes include the kappa, lambda, alpha, gamma, delta, epsilon, and mu constant region genes, as well as the myriad immunoglobulin variable region genes. Light chains are classified as either kappa or lambda. Heavy chains are classified as gamma, mu, alpha, delta, or epsilon, which in turn define the immunoglobulin classes, IgG, IgM, IgA, IgD and IgE, respectively. Typically, the antigen-binding region of an antibody will be most critical in specificity and affinity of binding.

[171] An exemplary immunoglobulin (antibody) structural unit comprises a tetramer. Each tetramer is composed of two identical pairs of polypeptide chains, each pair having one "light" (about 25 kD) and one "heavy" chain (about 50-70 kD). The N-terminus of each chain defines a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The terms variable light chain (V_L) and variable heavy chain (V_H) refer to these light and heavy chains respectively.

[172] Antibodies exist, e.g., as intact immunoglobulins or as a number of well-characterized fragments produced by digestion with various peptidases. Thus, for example, pepsin digests an antibody below the disulfide linkages in the hinge region to produce $F(ab)'_2$, a dimer of Fab which itself is a light chain joined to V_H-C_H1 by a disulfide bond. The $F(ab)'_2$ may be reduced under mild conditions to break the disulfide linkage in the hinge region, thereby converting the $F(ab)'_2$ dimer into an Fab' monomer. The Fab' monomer is essentially Fab with part of the hinge region (*see Fundamental Immunology* (Paul ed., 3d ed. 1993). While various antibody fragments are defined in terms of the

digestion of an intact antibody, one of skill will appreciate that such fragments may be synthesized *de novo* either chemically or by using recombinant DNA methodology. Thus, the term antibody, as used herein, also includes antibody fragments either produced by the modification of whole antibodies, or those synthesized *de novo* using recombinant DNA methodologies (e.g., single chain Fv) or those identified using phage display libraries (*see, e.g.*, McCafferty *et al.*, *Nature* 348:552-554 (1990))

[173] For preparation of antibodies, e.g., recombinant, monoclonal, or polyclonal antibodies, many technique known in the art can be used (*see, e.g.*, Kohler & Milstein, *Nature* 256:495-497 (1975); Kozbor *et al.*, *Immunology Today* 4: 72 (1983); Cole *et al.*, pp. 77-96 in *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc. (1985); Coligan, *Current Protocols in Immunology* (1991); Harlow & Lane, *Antibodies, A Laboratory Manual* (1988); and Goding, *Monoclonal Antibodies: Principles and Practice* (2d ed. 1986)). The genes encoding the heavy and light chains of an antibody of interest can be cloned from a cell, e.g., the genes encoding a monoclonal antibody can be cloned from a hybridoma and used to produce a recombinant monoclonal antibody. Gene libraries encoding heavy and light chaims of monoclonal antibodies can also be made from hybridoma or plasma cells. Random combinations of the heavy and light chain gene products generate a large pool of antibodies with different antigenic specificity (*see, e.g.*, Kuby, *Immunology* (3rd ed. 1997)). Techniques for the production of single chain antibodies or recombinant antibodies (U.S. Patent 4,946,778, U.S. Patent No. 4,816,567) can be adapted to produce antibodies to polypeptides of this invention. Also, transgenic mice, or other organisms such as other mammals, may be used to express humanized or human antibodies (*see, e.g.*, U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, Marks *et al.*, *Bio/Technology* 10:779-783 (1992); Lonberg *et al.*, *Nature* 368:856-859 (1994); Morrison, *Nature* 368:812-13 (1994); Fishwild *et al.*, *Nature Biotechnology* 14:845-51 (1996); Neuberger, *Nature Biotechnology* 14:826 (1996); and Lonberg & Huszar, *Intern. Rev. Immunol.* 13:65-93 (1995)). Alternatively, phage display technology can be used to identify antibodies and heteromeric Fab fragments that specifically bind to selected antigens (*see, e.g.*, McCafferty *et al.*, *Nature* 348:552-554 (1990); Marks *et al.*, *Biotechnology* 10:779-783 (1992)). Antibodies can also be made bispecific, i.e., able to recognize two different antigens (*see, e.g.*, WO 93/08829, Traunecker *et al.*, *EMBO J.* 10:3655-3659 (1991); and Suresh *et al.*, *Methods in Enzymology* 121:210 (1986)). Antibodies can also be heteroconjugates, e.g., two covalently joined antibodies, or immunotoxins (*see, e.g.*, U.S. Patent No. 4,676,980 , WO 91/00360; WO 92/200373; and EP 03089).

[174] Methods for humanizing or primatizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as import residues, which are typically taken from an import variable domain. Humanization can be essentially performed following the method of Winter and co-workers (*see, e.g.*, Jones *et al., Nature* 321:522-525 (1986); Riechmann *et al., Nature* 332:323-327 (1988); Verhoeyen *et al., Science* 239:1534-1536 (1988) and Presta, *Curr. Op. Struct. Biol.* 2:593-596 (1992)), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such humanized antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

[175] A "chimeric antibody" is an antibody molecule in which (a) the constant region, or a portion thereof, is altered, replaced or exchanged so that the antigen binding site (variable region) is linked to a constant region of a different or altered class, effector function and/or species, or an entirely different molecule which confers new properties to the chimeric antibody, e.g., an enzyme, toxin, hormone, growth factor, drug, etc.; or (b) the variable region, or a portion thereof, is altered, replaced or exchanged with a variable region having a different or altered antigen specificity.

[176] In one embodiment, the antibody is conjugated to an "effector" moiety. The effector moiety can be any number of molecules, including labeling moieties such as radioactive labels or fluorescent labels, or can be a therapeutic moiety. In one aspect the antibody modulates the activity of the protein.

[177] After the candidate agent has been added and the cells allowed to incubate for some period of time, the sample containing the target sequences to be analyzed is added to the biochip. If required, the target sequence is prepared using known techniques. For example, the sample may be treated to lyse the cells, using known lysis buffers, electroporation, etc., with purification and/or amplification such as PCR occurring as needed, as will be appreciated by those in the art. For example, an in vitro transcription with labels covalently attached to the nucleosides is done. Generally, the nucleic acids are labeled with biotin-FITC or PE, or with cy3 or cy5.

[178] In a preferred embodiment, the target sequence is labeled with, for example, a fluorescent, a chemiluminescent, a chemical, or a radioactive signal, to provide a means of detecting the target sequence's specific binding to a probe. The label also can be an enzyme, such as, alkaline phosphatase or horseradish peroxidase, which when provided with an appropriate substrate produces a product that can be detected. Alternatively, the label can be a labeled compound or small molecule, such as an enzyme inhibitor, that binds but is not catalyzed or altered by the enzyme. The label also can be a moiety or compound, such as, an epitope tag or biotin which specifically binds to streptavidin. For the example of biotin, the streptavidin is labeled as described above, thereby, providing a detectable signal for the bound target sequence. As known in the art, unbound labeled streptavidin is removed prior to analysis.

[179] As will be appreciated by those in the art, these assays can be direct hybridization assays or can comprise "sandwich assays", which include the use of multiple probes, as is generally outlined in U.S. Patent Nos. 5,681,702, 5,597,909, 5,545,730, 5,594,117, 5,591,584, 5,571,670, 5,580,731, 5,571,670, 5,591,584, 5,624,802, 5,635,352, 5,594,118, 5,359,100, 5,124,246 and 5,681,697, all of which are hereby incorporated by reference. In this embodiment, in general, the target nucleic acid is prepared as outlined above, and then added to the biochip comprising a plurality of nucleic acid probes, under conditions that allow the formation of a hybridization complex.

[180] A variety of hybridization conditions may be used in the present invention, including high, moderate and low stringency conditions as outlined above. The assays are generally run under stringency conditions which allows formation of the label probe hybridization complex only in the presence of target. Stringency can be controlled by altering a step parameter that is a thermodynamic variable, including, but not limited to, temperature, formamide concentration, salt concentration, chaotropic salt concentration pH, organic solvent concentration, etc.

[181] These parameters may also be used to control non-specific binding, as is generally outlined in U.S. Patent No. 5,681,697. Thus it may be desirable to perform certain steps at higher stringency conditions to reduce non-specific binding.

[182] The reactions outlined herein may be accomplished in a variety of ways, as will be appreciated by those in the art. Components of the reaction may be added simultaneously, or sequentially, in any order, with preferred embodiments outlined below. In addition, the reaction may include a variety of other reagents may be included in the assays. These include reagents like salts, buffers, neutral proteins, e.g. albumin, detergents, etc which

may be used to facilitate optimal hybridization and detection, and/or reduce non-specific or background interactions. Also reagents that otherwise improve the efficiency of the assay, such as protease inhibitors, nuclease inhibitors, anti-microbial agents, etc., may be used, depending on the sample preparation methods and purity of the target.

[183] Once the assay is run, the data is analyzed to determine the expression levels, and changes in expression levels as between states, of individual genes, forming a gene expression profile.

[184] The screens are done to identify drugs or bioactive agents that modulate the colorectal cancer phenotype. Specifically, there are several types of screens that can be run. A preferred embodiment is in the screening of candidate agents that can induce or suppress a particular expression profile, thus preferably generating the associated phenotype. That is, candidate agents that can mimic or produce an expression profile in colorectal cancer similar to the expression profile of normal colon tissue is expected to result in a suppression of the colorectal cancer phenotype. Thus, in this embodiment, mimicking an expression profile, or changing one profile to another, is the goal.

[185] In a preferred embodiment, as for the diagnosis and prognosis applications, having identified the differentially expressed genes important in any one state, screens can be run to alter the expression of the genes individually. That is, screening for modulation of regulation of expression of a single gene can be done; that is, rather than try to mimic all or part of an expression profile, screening for regulation of individual genes can be done. Thus, for example, particularly in the case of target genes whose presence or absence is unique between two states, screening is done for modulators of the target gene expression.

[186] In a preferred embodiment, screening is done to alter the biological function of the expression product of the differentially expressed gene. Again, having identified the importance of a gene in a particular state, screening for agents that bind and/or modulate the biological activity of the gene product can be run as is more fully outlined below.

[187] Thus, screening of candidate agents that modulate the colorectal cancer phenotype either at the gene expression level or the protein level can be done.

[188] In addition screens can be done for novel genes that are induced in response to a candidate agent. After identifying a candidate agent based upon its ability to suppress a colorectal cancer expression pattern leading to a normal expression pattern, or modulate a single colorectal cancer gene expression profile so as to mimic the expression of the gene from normal tissue, a screen as described above can be performed to identify genes

that are specifically modulated in response to the agent. Comparing expression profiles between normal tissue and agent treated colorectal cancer tissue reveals genes that are not expressed in normal tissue or colorectal cancer tissue, but are expressed in agent treated tissue. These agent specific sequences can be identified and used by any of the methods described herein for colorectal cancer genes or proteins. In particular these sequences and the proteins they encode find use in marking or identifying agent treated cells. In addition, antibodies can be raised against the agent induced proteins and used to target novel therapeutics to the treated colorectal cancer tissue sample.

[189] Thus, in one embodiment, a candidate agent is administered to a population of colorectal cancer cells, that thus has an associated colorectal cancer expression profile. By "administration" or "contacting" herein is meant that the candidate agent is added to the cells in such a manner as to allow the agent to act upon the cell, whether by uptake and intracellular action, or by action at the cell surface. In some embodiments, nucleic acid encoding a proteinaceous candidate agent (i.e. a peptide) may be put into a viral construct such as a retroviral construct and added to the cell, such that expression of the peptide agent is accomplished; see PCT US97/01019, hereby expressly incorporated by reference.

[190] Once the candidate agent has been administered to the cells, the cells can be washed if desired and are allowed to incubate under preferably physiological conditions for some period of time. The cells are then harvested and a new gene expression profile is generated, as outlined herein.

[191] Thus, for example, colorectal cancer tissue may be screened for agents that reduce or suppress the colorectal cancer phenotype. A change in at least one gene of the expression profile indicates that the agent has an effect on colorectal cancer activity. By defining such a signature for the colorectal cancer phenotype, screens for new drugs that alter the phenotype can be devised. With this approach, the drug target need not be known and need not be represented in the original expression screening platform, nor does the level of transcript for the target protein need to change.

[192] In a preferred embodiment, as outlined above, screens may be done on individual genes and gene products (proteins). That is, having identified a particular differentially expressed gene as important in a particular state, screening of modulators of either the expression of the gene or the gene product itself can be done. The gene products of differentially expressed genes are sometimes referred to herein as "colorectal cancer modulator proteins". The colorectal cancer modulator protein may be a fragment, or

alternatively, be the full length protein to a fragment shown herein. Preferably, the colorectal cancer modulator protein is a fragment of approximately 14 to 24 amino acids long. More preferably the fragment is a soluble fragment.

[193] In a preferred embodiment, the fragment is charged and from the c-terminus. In one embodiment, the c-terminus of the fragment is kept as a free acid and the n-terminus is a free amine to aid in coupling, i.e., to cysteine. In another embodiment, the fragment is an internal peptide overlapping hydrophilic stretch the protein. In a preferred embodiment, the termini is blocked. In another preferred embodiment, the fragment is a novel fragment from the N-terminal. In one embodiment, the fragment excludes sequence outside of the N-terminal, in another embodiment, the fragment includes at least a portion of the N-terminal. "N-terminal" is used interchangeably herein with "N-terminus" which is further described above.

[194] In one embodiment the colorectal cancer proteins are conjugated to an immunogenic agent as discussed herein. In one embodiment the colorectal cancer protein is conjugated to BSA.

[195] Thus, in a preferred embodiment, screening for modulators of expression of specific genes can be done. This will be done as outlined above, but in general the expression of only one or a few genes are evaluated.

[196] In a preferred embodiment, screens are designed to first find candidate agents that can bind to differentially expressed proteins, and then these agents may be used in assays that evaluate the ability of the candidate agent to modulate differentially expressed activity. Thus, as will be appreciated by those in the art, there are a number of different assays which may be run; binding assays and activity assays.

[197] In a preferred embodiment, binding assays are done. In general, purified or isolated gene product is used; that is, the gene products of one or more differentially expressed nucleic acids are made. In general, this is done as is known in the art. For example, antibodies are generated to the protein gene products, and standard immunoassays are run to determine the amount of protein present. Alternatively, cells comprising the colorectal cancer proteins can be used in the assays.

[198] Thus, in a preferred embodiment, the methods comprise combining a colorectal cancer protein and a candidate bioactive agent, and determining the binding of the candidate agent to the colorectal cancer protein. Preferred embodiments utilize the human colorectal cancer protein, although other mammalian proteins may also be used, for example

for the development of animal models of human disease. In some embodiments, as outlined herein, variant or derivative colorectal cancer proteins may be used.

[199] Generally, in a preferred embodiment of the methods herein, the colorectal cancer protein or the candidate agent is non-diffusably bound to an insoluble support having isolated sample receiving areas (e.g. a microtiter plate, an array, etc.). The insoluble supports may be made of any composition to which the compositions can be bound, is readily separated from soluble material, and is otherwise compatible with the overall method of screening. The surface of such supports may be solid or porous and of any convenient shape. Examples of suitable insoluble supports include microtiter plates, arrays, membranes and beads. These are typically made of glass, plastic (e.g., polystyrene), polysaccharides, nylon or nitrocellulose, teflon, etc. Microtiter plates and arrays are especially convenient because a large number of assays can be carried out simultaneously, using small amounts of reagents and samples. The particular manner of binding of the composition is not crucial so long as it is compatible with the reagents and overall methods of the invention, maintains the activity of the composition and is nondiffusable. Preferred methods of binding include the use of antibodies (which do not sterically block either the ligand binding site or activation sequence when the protein is bound to the support), direct binding to "sticky" or ionic supports, chemical crosslinking, the synthesis of the protein or agent on the surface, etc. Following binding of the protein or agent, excess unbound material is removed by washing. The sample receiving areas may then be blocked through incubation with bovine serum albumin (BSA), casein or other innocuous protein or other moiety.

[200] In a preferred embodiment, the colorectal cancer protein is bound to the support, and a candidate bioactive agent is added to the assay. Alternatively, the candidate agent is bound to the support and the colorectal cancer protein is added. Novel binding agents include specific antibodies, non-natural binding agents identified in screens of chemical libraries, peptide analogs, etc. Of particular interest are screening assays for agents that have a low toxicity for human cells. A wide variety of assays may be used for this purpose, including labeled in vitro protein-protein binding assays, electrophoretic mobility shift assays, immunoassays for protein binding, functional assays (phosphorylation assays, etc.) and the like.

[201] The determination of the binding of the candidate bioactive agent to the colorectal cancer protein may be done in a number of ways. In a preferred embodiment, the candidate bioactive agent is labeled, and binding determined directly. For example, this may be done by attaching all or a portion of the colorectal cancer protein to a solid support,

adding a labeled candidate agent (for example a fluorescent label), washing off excess reagent, and determining whether the label is present on the solid support. Various blocking and washing steps may be utilized as is known in the art.

[202] By "labeled" herein is meant that the compound is either directly or indirectly labeled with a label which provides a detectable signal, e.g. radioisotope, fluorescers, enzyme, antibodies, particles such as magnetic particles, chemiluminescers, or specific binding molecules, etc. Specific binding molecules include pairs, such as biotin and streptavidin, digoxin and antidigoxin etc. For the specific binding members, the complementary member would normally be labeled with a molecule which provides for detection, in accordance with known procedures, as outlined above. The label can directly or indirectly provide a detectable signal.

[203] In some embodiments, only one of the components is labeled. For example, the proteins (or proteinaceous candidate agents) may be labeled at tyrosine positions using 125I, or with fluorophores. Alternatively, more than one component may be labeled with different labels; using ^{125}I for the proteins, for example, and a fluorophor for the candidate agents.

[204] In a preferred embodiment, the binding of the candidate bioactive agent is determined through the use of competitive binding assays. In this embodiment, the competitor is a binding moiety known to bind to the target molecule (i.e. colorectal cancer), such as an antibody, peptide, binding partner, ligand, etc. Under certain circumstances, there may be competitive binding as between the bioactive agent and the binding moiety, with the binding moiety displacing the bioactive agent.

[205] In one embodiment, the candidate bioactive agent is labeled. Either the candidate bioactive agent, or the competitor, or both, is added first to the protein for a time sufficient to allow binding, if present. Incubations may be performed at any temperature which facilitates optimal activity, typically between 4 and 40°C. Incubation periods are selected for optimum activity, but may also be optimized to facilitate rapid high through put screening. Typically between 0.1 and 1 hour will be sufficient. Excess reagent is generally removed or washed away. The second component is then added, and the presence or absence of the labeled component is followed, to indicate binding.

[206] In a preferred embodiment, the competitor is added first, followed by the candidate bioactive agent. Displacement of the competitor is an indication that the candidate bioactive agent is binding to the colorectal cancer protein and thus is capable of binding to, and potentially modulating, the activity of the colorectal cancer protein. In this

embodiment, either component can be labeled. Thus, for example, if the competitor is labeled, the presence of label in the wash solution indicates displacement by the agent. Alternatively, if the candidate bioactive agent is labeled, the presence of the label on the support indicates displacement.

[207] In an alternative embodiment, the candidate bioactive agent is added first, with incubation and washing, followed by the competitor. The absence of binding by the competitor may indicate that the bioactive agent is bound to the colorectal cancer protein with a higher affinity. Thus, if the candidate bioactive agent is labeled, the presence of the label on the support, coupled with a lack of competitor binding, may indicate that the candidate agent is capable of binding to the colorectal cancer protein.

[208] In a preferred embodiment, the methods comprise differential screening to identity bioactive agents that are capable of modulating the activity of the colorectal cancer proteins. In this embodiment, the methods comprise combining a colorectal cancer protein and a competitor in a first sample. A second sample comprises a candidate bioactive agent, a colorectal cancer protein and a competitor. The binding of the competitor is determined for both samples, and a change, or difference in binding between the two samples indicates the presence of an agent capable of binding to the colorectal cancer protein and potentially modulating its activity. That is, if the binding of the competitor is different in the second sample relative to the first sample, the agent is capable of binding to the colorectal cancer protein.

[209] Alternatively, a preferred embodiment utilizes differential screening to identify drug candidates that bind to the native colorectal cancer protein, but cannot bind to modified colorectal cancer proteins. The structure of the colorectal cancer protein may be modeled, and used in rational drug design to synthesize agents that interact with that site. Drug candidates that affect colorectal cancer bioactivity are also identified by screening drugs for the ability to either enhance or reduce the activity of the protein.

[210] Positive controls and negative controls may be used in the assays. Preferably all control and test samples are performed in at least triplicate to obtain statistically significant results. Incubation of all samples is for a time sufficient for the binding of the agent to the protein. Following incubation, all samples are washed free of non-specifically bound material and the amount of bound, generally labeled agent determined. For example, where a radiolabel is employed, the samples may be counted in a scintillation counter to determine the amount of bound compound.

[211] A variety of other reagents may be included in the screening assays. These include reagents like salts, neutral proteins, e.g. albumin, detergents, etc which may be used to facilitate optimal protein-protein binding and/or reduce non-specific or background interactions. Also reagents that otherwise improve the efficiency of the assay, such as protease inhibitors, nuclease inhibitors, anti-microbial agents, etc., may be used. The mixture of components may be added in any order that provides for the requisite binding.

[212] Screening for agents that modulate the activity of colorectal cancer proteins may also be done. In a preferred embodiment, methods for screening for a bioactive agent capable of modulating the activity of colorectal cancer proteins comprise the steps of adding a candidate bioactive agent to a sample of colorectal cancer proteins, as above, and determining an alteration in the biological activity of colorectal cancer proteins. "Modulating the activity of colorectal cancer " includes an increase in activity, a decrease in activity, or a change in the type or kind of activity present. Thus, in this embodiment, the candidate agent should both bind to colorectal cancer proteins (although this may not be necessary), and alter its biological or biochemical activity as defined herein. The methods include both in vitro screening methods, as are generally outlined above, and in vivo screening of cells for alterations in the presence, distribution, activity or amount of colorectal cancer proteins.

[213] Thus, in this embodiment, the methods comprise combining a colorectal cancer sample and a candidate bioactive agent, and evaluating the effect on colorectal cancer activity. By "colorectal cancer activity" or grammatical equivalents herein is meant one of the colorectal cancer 's biological activities, including, but not limited to, cell division, preferably in colon tissue, cell proliferation, tumor growth, transformation of cells. In one embodiment, colorectal cancer activity includes activation of a gene identified by a nucleic acid of Table 1. An inhibitor of colorectal cancer activity is the inhibition of any one or more colorectal cancer activities.

[214] In a preferred embodiment, the activity of the colorectal cancer protein is increased; in another preferred embodiment, the activity of the colorectal cancer protein is decreased. Thus, bioactive agents that are antagonists are preferred in some embodiments, and bioactive agents that are agonists may be preferred in other embodiments.

[215] In a preferred embodiment, the invention provides methods for screening for bioactive agents capable of modulating the activity of a colorectal cancer protein. The methods comprise adding a candidate bioactive agent, as defined above, to a cell comprising colorectal cancer proteins. Preferred cell types include almost any cell. The

cells contain a recombinant nucleic acid that encodes a colorectal cancer protein. In a preferred embodiment, a library of candidate agents are tested on a plurality of cells.

[216] In one aspect, the assays are evaluated in the presence or absence or previous or subsequent exposure of physiological signals, for example hormones, antibodies, peptides, antigens, cytokines, growth factors, action potentials, pharmacological agents including chemotherapeutics, radiation, carcinogenics, or other cells (i.e. cell-cell contacts). In another example, the determinations are determined at different stages of the cell cycle process.

[217] In this way, bioactive agents are identified. Compounds with pharmacological activity are able to enhance or interfere with the activity of the colorectal cancer protein. In one embodiment, "colorectal cancer protein activity" as used herein includes at least one of the following: colorectal cancer activity, binding to the colorectal cancer protein, activation of the colorectal cancer protein or activation of substrates of the colorectal cancer protein by the colorectal cancer protein. In one embodiment, colorectal cancer activity is defined as the unregulated proliferation of colon tissue, or the growth of cancer in colon tissue. In one aspect, colorectal cancer activity as defined herein is related to the activity of the colorectal cancer protein in the upregulation of the colorectal cancer protein in colon cancer tissue.

[218] In another embodiment, colorectal cancer protein activity includes at least one of the following: colorectal cancer activity, binding to the CBF9 nucleic acid or poly peptide of Table 2 or binding toa nucleic acid of Table 1, or a peptide encoded by a nucleic acid of Table 1 or activation of substrates of the gene products identified by a nucleic acid of Table 1 or substrates of CBF9, which is shown in Table 2. In one aspect, colorectal cancer activity as defined herein is related to the activity of genes defined by the nucleic acids of Table 1 or of CBF9 as defined in Table 2, in colon cancer tissue.

[219] In one embodiment, a method of inhibiting colon cancer cell division is provided. The method comprises administration of a colorectal cancer inhibitor.

[220] In another embodiment, a method of inhibiting tumor growth is provided. The method comprises administration of a colorectal cancer inhibitor.

[221] In a further embodiment, methods of treating cells or individuals with cancer are provided. The method comprises administration of a colorectal cancer inhibitor.

[222] In one embodiment, a colorectal cancer inhibitor is an antibody as discussed above. In another embodiment, the colorectal cancer inhibitor is an antisense molecule. Antisense molecules as used herein include antisense or sense oligonucleotides

comprising a singe-stranded nucleic acid sequence (either RNA or DNA) capable of binding to target mRNA (sense) or DNA (antisense) sequences for colorectal cancer molecules. A preferred antisense molecule is for the colorectal cancer sequences referenced in Table 1 or Table 2, or for a ligand or activator thereof. Antisense or sense oligonucleotides, according to the present invention, comprise a fragment generally at least about 14 nucleotides, preferably from about 14 to 30 nucleotides. The ability to derive an antisense or a sense oligonucleotide, based upon a cDNA sequence encoding a given protein is described in, for example, Stein and Cohen (Cancer Res. 48:2659, 1988) and van der Krol et al. (BioTechniques 6:958, 1988).

[223] Antisense molecules may be introduced into a cell containing the target nucleotide sequence by formation of a conjugate with a ligand binding molecule, as described in WO 91/04753. Suitable ligand binding molecules include, but are not limited to, cell surface receptors, growth factors, other cytokines, or other ligands that bind to cell surface receptors. Preferably, conjugation of the ligand binding molecule does not substantially interfere with the ability of the ligand binding molecule to bind to its corresponding molecule or receptor, or block entry of the sense or antisense oligonucleotide or its conjugated version into the cell. Alternatively, a sense or an antisense oligonucleotide may be introduced into a cell containing the target nucleic acid sequence by formation of an oligonucleotide-lipid complex, as described in WO 90/10448. It is understood that the use of antisense molecules or knock out and knock in models may also be used in screening assays as discussed above, in addition to methods of treatment.

[224] The compounds having the desired pharmacological activity may be administered in a physiologically acceptable carrier to a host, as previously described. The agents may be administered in a variety of ways, orally, parenterally e.g., subcutaneously, intraperitoneally, intravascularly, etc. Depending upon the manner of introduction, the compounds may be formulated in a variety of ways. The concentration of therapeutically active compound in the formulation may vary from about 0.1-100 wt.%. The agents may be administered alone or in combination with other treatments, i.e., radiation.

[225] The pharmaceutical compositions can be prepared in various forms, such as granules, tablets, pills, suppositories, capsules, suspensions, salves, lotions and the like. Pharmaceutical grade organic or inorganic carriers and/or diluents suitable for oral and topical use can be used to make up compositions containing the therapeutically-active compounds. Diluents known to the art include aqueous media, vegetable and animal oils and fats. Stabilizing agents, wetting and emulsifying agents, salts for varying the osmotic

pressure or buffers for securing an adequate pH value, and skin penetration enhancers can be used as auxiliary agents.

[226] Without being bound by theory, it appears that the various colorectal cancer sequences are important in colorectal cancer. Accordingly, disorders based on mutant or variant colorectal cancer genes may be determined. In one embodiment, the invention provides methods for identifying cells containing variant colorectal cancer genes comprising determining all or part of the sequence of at least one endogeneous colorectal cancer genes in a cell. As will be appreciated by those in the art, this may be done using any number of sequencing techniques. In a preferred embodiment, the invention provides methods of identifying the colorectal cancer genotype of an individual comprising determining all or part of the sequence of at least one colorectal cancer gene of the individual. This is generally done in at least one tissue of the individual, and may include the evaluation of a number of tissues or different samples of the same tissue. The method may include comparing the sequence of the sequenced colorectal cancer gene to a known colorectal cancer gene, i.e. a wild-type gene.

[227] The sequence of all or part of the colorectal cancer gene can then be compared to the sequence of a known colorectal cancer gene to determine if any differences exist. This can be done using any number of known homology programs, such as Bestfit, etc. In a preferred embodiment, the presence of a a difference in the sequence between the colorectal cancer gene of the patient and the known colorectal cancer gene is indicative of a disease state or a propensity for a disease state, as outlined herein.

[228] In a preferred embodiment, the colorectal cancer genes are used as probes to determine the number of copies of the colorectal cancer gene in the genome.

[229] In another preferred embodiment colorectal cancer genes are used as probed to determine the chromosomal localization of the colorectal cancer genes. Information such as chromosomal localization finds use in providing a diagnosis or prognosis in particular when chromosomal abnormalities such as translocations, and the like are identified in colorectal cancer gene loci.

[230] Thus, in one embodiment, methods of modulating colorectal cancer in cells or organisms are provided. In one embodiment, the methods comprise administering to a cell an anti-colorectal cancer antibody that reduces or eliminates the biological activity of an endogeneous colorectal cancer protein. Alternatively, the methods comprise administering to a cell or organism a recombinant nucleic acid encoding a colorectal cancer protein. As will be appreciated by those in the art, this may be accomplished in any number

of ways. In a preferred embodiment, for example when the colorectal cancer sequence is down-regulated in colorectal cancer , the activity of the colorectal cancer gene is increased by increasing the amount of colorectal cancer in the cell, for example by overexpressing the endogeneous colorectal cancer or by administering a gene encoding the colorectal cancer sequence, using known gene-therapy techniques, for example. In a preferred embodiment, the gene therapy techniques include the incorporation of the erogenous gene using enhanced homologous recombination (EHR), for example as described in PCT/US93/03868, hereby incorporated by reference in its entirety. Alternatively, for example when the colorectal cancer sequence is up-regulated in colorectal cancer , the activity of the endogeneous colorectal cancer gene is decreased, for example by the administration of a colorectal cancer antisense nucleic acid.

[231] In one embodiment, the colorectal cancer proteins of the present invention may be used to generate polyclonal and monoclonal antibodies to colorectal cancer proteins, which are useful as described herein. Similarly, the colorectal cancer proteins can be coupled, using standard technology, to affinity chromatography columns. These columns may then be used to purify colorectal cancer antibodies. In a preferred embodiment, the antibodies are generated to epitopes unique to a colorectal cancer protein; that is, the antibodies show little or no cross-reactivity to other proteins. These antibodies find use in a number of applications. For example, the colorectal cancer antibodies may be coupled to standard affinity chromatography columns and used to purify colorectal cancer proteins. The antibodies may also be used as blocking polypeptides, as outlined above, since they will specifically bind to the colorectal cancer protein.

[232] In one embodiment, a therapeutically effective dose of a colorectal cancer or modulator thereof is administered to a patient. By "therapeutically effective dose" herein is meant a dose that produces the effects for which it is administered. The exact dose will depend on the purpose of the treatment, and will be ascertainable by one skilled in the art using known techniques. As is known in the art, adjustments for colorectal cancer degradation, systemic versus localized delivery, and rate of new protease synthesis, as well as the age, body weight, general health, sex, diet, time of administration, drug interaction and the severity of the condition may be necessary, and will be ascertainable with routine experimentation by those skilled in the art.

[233] A "patient" for the purposes of the present invention includes both humans and other animals, particularly mammals, and organisms. Thus the methods are

applicable to both human therapy and veterinary applications. In the preferred embodiment the patient is a mammal, and in the most preferred embodiment the patient is human.

[234] The administration of the colorectal cancer proteins and modulators of the present invention can be done in a variety of ways as discussed above, including, but not limited to, orally, subcutaneously, intravenously, intranasally, transdermally, intraperitoneally, intramuscularly, intrapulmonary, vaginally, rectally, or intraocularly. In some instances, for example, in the treatment of wounds and inflammation, the colorectal cancer proteins and modulators may be directly applied as a solution or spray.

[235] The pharmaceutical compositions of the present invention comprise a colorectal cancer protein in a form suitable for administration to a patient. In the preferred embodiment, the pharmaceutical compositions are in a water soluble form, such as being present as pharmaceutically acceptable salts, which is meant to include both acid and base addition salts. "Pharmaceutically acceptable acid addition salt" refers to those salts that retain the biological effectiveness of the free bases and that are not biologically or otherwise undesirable, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and organic acids such as acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid and the like. "Pharmaceutically acceptable base addition salts" include those derived from inorganic bases such as sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Particularly preferred are the ammonium, potassium, sodium, calcium, and magnesium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, and ethanolamine.

[236] The pharmaceutical compositions may also include one or more of the following: carrier proteins such as serum albumin; buffers; fillers such as microcrystalline cellulose, lactose, corn and other starches; binding agents; sweeteners and other flavoring agents; coloring agents; and polyethylene glycol. Additives are well known in the art, and are used in a variety of formulations.

[237] In a preferred embodiment, colorectal cancer proteins and modulators are administered as therapeutic agents, and can be formulated as outlined above. Similarly,

colorectal cancer genes (including both the full-length sequence, partial sequences, or regulatory sequences of the colorectal cancer coding regions) can be administered in gene therapy applications, as is known in the art. These colorectal cancer genes can include antisense applications, either as gene therapy (i.e. for incorporation into the genome) or as antisense compositions, as will be appreciated by those in the art.

[238] In a preferred embodiment, colorectal cancer genes are administered as DNA vaccines, either single genes or combinations of colorectal cancer genes. Naked DNA vaccines are generally known in the art. Brower, Nature Biotechnology, 16:1304-1305 (1998).

[239] In one embodiment, colorectal cancer genes of the present invention are used as DNA vaccines. Methods for the use of genes as DNA vaccines are well known to one of ordinary skill in the art, and include placing a colorectal cancer gene or portion of a colorectal cancer gene under the control of a promoter for expression in a colorectal cancer patient. The colorectal cancer gene used for DNA vaccines can encode full-length colorectal cancer proteins, but more preferably encodes portions of the colorectal cancer proteins including peptides derived from the colorectal cancer protein. In a preferred embodiment a patient is immunized with a DNA vaccine comprising a plurality of nucleotide sequences derived from a colorectal cancer gene. Similarly, it is possible to immunize a patient with a plurality of colorectal cancer genes or portions thereof as defined herein. Without being bound by theory, expression of the polypeptide encoded by the DNA vaccine, cytotoxic T-cells, helper T-cells and antibodies are induced which recognize and destroy or eliminate cells expressing colorectal cancer proteins.

[240] In a preferred embodiment, the DNA vaccines include a gene encoding an adjuvant molecule with the DNA vaccine. Such adjuvant molecules include cytokines that increase the immunogenic response to the colorectal cancer polypeptide encoded by the DNA vaccine. Additional or alternative adjuvants are known to those of ordinary skill in the art and find use in the invention.

[241] In another preferred embodiment colorectal cancer genes find use in generating animal models of colorectal cancer . As is appreciated by one of ordinary skill in the art, when the colorectal cancer gene identified is repressed or diminished in colorectal cancer tissue, gene therapy technology wherein antisense RNA directed to the colorectal cancer gene will also diminish or repress expression of the gene. An animal generated as such serves as an animal model of colorectal cancer that finds use in screening bioactive drug candidates. Similarly, gene knockout technology, for example as a result of

homologous recombination with an appropriate gene targeting vector, will result in the absence of the colorectal cancer protein. When desired, tissue-specific expression or knockout of the colorectal cancer protein may be necessary.

[242] It is also possible that the colorectal cancer protein is overexpressed in colorectal cancer. As such, transgenic animals can be generated that overexpress the colorectal cancer protein. Depending on the desired expression level, promoters of various strengths can be employed to express the transgene. Also, the number of copies of the integrated transgene can be determined and compared for a determination of the expression level of the transgene. Animals generated by such methods find use as animal models of colorectal cancer and are additionally useful in screening for bioactive molecules to treat colorectal cancer.

EXAMPLES

[243] It is understood that the examples described herein in no way serve to limit the true scope of this invention, but rather are presented for illustrative purposes. All references and sequences of accession numbers cited herein are incorporated by reference in their entirety.

[244] Example 1

Tissue Preparation, Labeling Chips, and Fingerprints

[245] Purify total RNA from tissue using TRIzol Reagent

[246] Estimate tissue weight. Homogenize tissue samples in 1ml of TRIzol per 50mg of tissue using a Polytron 3100 homogenizer. The generator/probe used depends upon the tissue size. A generator that is too large for the amount of tissue to be homogenized will cause a loss of sample and lower RNA yield. Use the 20mm generator for tissue weighing more than 0.6g. If the working volume is greater than 2ml, then homogenize tissue in a 15ml polypropylene tube (Falcon 2059). Fill tube no greater than 10ml.

HOMOGENIZATION

[247] Before using generator, it should have been cleaned after last usage by running it through soapy H20 and rinsing thoroughly. Run through with EtOH to sterilize. Keep tissue frozen until ready. Add TRIzol directly to frozen tissue then homogenize.

[248] Following homogenization, remove insoluble material from the homogenate by centrifugation at 7500 x g for 15 min. in a Sorvall superspeed or 12,000 x g for 10 min. in an Eppendorf centrifuge at 4oC. Transfer the cleared homogenate to a new tube(s). The samples may be frozen now at -60 to -70oC (and kept for at least one month) or you may continue with the purification.

PHASE SEPARATION

[249] Incubate the homogenized samples for 5 minutes at room temperature.

[250] Add 0.2ml of chloroform per 1ml of TRIzol reagent used in the original homogenization.

[251] Cap tubes securely and shake tubes vigorously by hand (do not vortex) for 15 seconds.

[252] Incubate samples at room temp. for 2-3 minutes. Centrifuge samples at 6500rpm in a Sorvall superspeed for 30 min. at 4oC. (You may spin at up to 12,000 x g for 10 min. but you risk breaking your tubes in the centrifuge.)

RNA PRECIPITATION

[253] Transfer the aqueous phase to a fresh tube. Save the organic phase if isolation of DNA or protein is desired. Add 0.5ml of isopropyl alcohol per 1ml of TRIzol reagent used in the original homogenization. Cap tubes securely and invert to mix. Incubate samples at room temp. for 10 minutes. Centrifuge samples at 6500rpm in Sorvall for 20min. at 4oC.

RNA WASH

[254] Pour off the supernate. Wash pellet with cold 75% ethanol. Use 1ml of 75% ethanol per 1ml of TRIzol reagent used in the initial homogenization. Cap tubes securely and invert several times to loosen pellet. (Do not vortex). Centrifuge at <8000rpm (<7500 x g) for 5 minutes at 4oC.

[255] Pour off the wash. Carefully transfer pellet to an eppendorf tube (let it slide down the tube into the new tube and use a pipet tip to help guide it in if necessary). Depending on the volumes you are working with, you can decide what size tube(s) you want to precipitate the RNA in. When I tried leaving the RNA in the large 15ml tube, it took so long to dry (i.e. it did not dry) that I eventually had to transfer it to a smaller tube. Let pellet

dry in hood. Resuspend RNA in an appropriate volume of DEPC H20. Try for 2-5ug/ul. Take absorbance readings.

[256] Purify poly A+ mRNA from total RNA or clean up total RNA with Qiagen' s RNeasy kit

[257] Purification of poly A+ mRNA from total RNA. Heat oligotex suspension to 37oC and mix immediately before adding to RNA. Incubate Elution Buffer at 70oC. Warm up 2 x Binding Buffer at 65oC if there is precipitate in the buffer. Mix total RNA with DEPC-treated water, 2 x Binding Buffer, and Oligotex according to Table 2 on page 16 of the Oligotex Handbook. Incubate for 3 minutes at 65oC. Incubate for 10 minutes at room temperature.

[258] Centrifuge for 2 minutes at 14,000 to 18,000 g. If centrifuge has a "soft setting," then use it. Remove supernatant without disturbing Oligotex pellet. A little bit of solution can be left behind to reduce the loss of Oligotex. Save sup until certain that satisfactory binding and elution of poly A+ mRNA has occurred.

[259] Gently resuspend in Wash Buffer OW2 and pipet onto spin column. Centrifuge the spin column at full speed (soft setting if possible) for 1 minute.

[260] Transfer spin column to a new collection tube and gently resuspend in Wash Buffer OW2 and centrifuge as describe herein.

[261] Transfer spin column to a new tube and elute with 20 to 100 ul of preheated (70oC) Elution Buffer. Gently resuspend Oligotex resin by pipetting up and down. Centrifuge as above. Repeat elution with fresh elution buffer or use first eluate to keep the elution volume low.

[262] Read absorbance, using diluted Elution Buffer as the blank.

[263] Before proceeding with cDNA synthesis, the mRNA must be precipitated. Some component leftover or in the Elution Buffer from the Oligotex purification procedure will inhibit downstream enzymatic reactions of the mRNA.

Ethanol Precipitation

[264] Add 0.4 vol. of 7.5 M NH4OAc + 2.5 vol. of cold 100% ethanol. Precipitate at -20oC 1 hour to overnight (or 20-30 min. at -70oC). Centrifuge at 14,000-16,000 x g for 30 minutes at 4oC. Wash pellet with 0.5ml of 80%ethanol (-20oC) then centrifuge at 14,000-16,000 x g for 5 minutes at room temperature. Repeat 80% ethanol wash. Dry the last bit of ethanol from the pellet in the hood. (Do not speed vacuum). Suspend pellet in DEPC H20 at 1ug/ul concentration.

Clean up total RNA using Qiagen's RNeasy kit

[265] Add no more than 100ug to an RNeasy column. Adjust sample to a volume of 100ul with RNase-free water. Add 350ul Buffer RLT then 250ul ethanol (100%) to the sample. Mix by pipetting (do not centrifuge) then apply sample to an RNeasy mini spin column. Centrifuge for 15 sec at >10,000rpm. If concerned about yield, re-apply flowthrough to column and centrifuge again.

[266] Transfer column to a new 2-ml collection tube. Add 500ul Buffer RPE and centrifuge for 15 sec at >10,000rpm. Discard flowthrough. Add 500ul Buffer RPE and centrifuge for 15 sec at >10,000rpm. Discard flowthrough then centrifuge for 2 min at maximum speed to dry column membrane. Transfer column to a new 1.5-ml collection tube and apply 30-50ul of RNase-free water directly onto column membrane. Centrifuge 1 min at >10,000rpm. Repeat elution.

[267] Take absorbance reading. If necessary, ethanol precipitate with ammonium acetate and 2.5X volume 100% ethanol.

[268] Make cDNA using Gibco's "SuperScript Choice System for cDNA Synthesis" kit

First Strand cDNA Synthesis

[269] Use 5ug of total RNA or 1ug of polyA+ mRNA as starting material. For total RNA, use 2ul of SuperScript RT. For polyA+ mRNA, use 1ul of SuperScript RT. Final volume of first strand synthesis mix is 20ul. RNA must be in a volume no greater than 10ul. Incubate RNA with 1ul of 100pmol T7-T24 oligo for 10 min at 70C. On ice, add 7 ul of: 4ul 5X 1st Strand Buffer, 2ul of 0.1M DTT, and 1 ul of 10mM dNTP mix. Incubate at 37C for 2 min then add SuperScript RT

Incubate at 37C for 1 hour.

Second Strand Synthesis

Place 1st strand reactions on ice.

Add: 91ul DEPC H20

30ul 5X 2nd Strand Buffer

3ul 10mM dNTP mix

1ul 10U/ul E.coli DNA Ligase

4ul 10U/ul E.coli DNA Polymerase

1ul 2U/ul RNase H

[270] Make the above into a mix if there are more than 2 samples. Mix and incubate 2 hours at 16C.

[271] Add 2ul T4 DNA Polymerase. Incubate 5 min at 16C. Add 10ul of 0.5M EDTA

[272] Clean up cDNA

[273] Phenol:Chloroform:Isoamyl Alcohol (25:24:1) purification using Phase-Lock gel tubes:

[274] Centrifuge PLG tubes for 30 sec at maximum speed. Transfer cDNA mix to PLG tube. Add equal volume of phenol:chloroform:isamyl alcohol and shake vigorously (do not vortex). Centrifuge 5 minutes at maximum speed. Transfer top aqueous solution to a new tube. Ethanol precipitate: add 7.5X 5M NH4Oac and 2.5X volume of 100% ethanol. Centrifuge immediately at room temp. for 20 min, maximum speed. Remove sup then wash pellet 2X with cold 80% ethanol. Remove as much ethanol wash as possible then let pellet air dry. Resuspend pellet in 3ul RNase-free water.

In vitro Transcription (IVT) and labeling with biotin

Pipet 1.5ul of cDNA into a thin-wall PCR tube.

Make NTP labeling mix:

Combine at room temperature: 2ul T7 10xATP (75mM) (Ambion)

2ul T7 10xGTP (75mM) (Ambion)

1.5ul T7 10xCTP (75mM) (Ambion)

1.5ul T7 10xUTP (75mM) (Ambion)

3.75ul 10mM Bio-11-UTP (Boehringer-Mannheim/Roche or Enzo)

3.75ul 10mM Bio-16-CTP (Enzo)

2ul 10x T7 transcription buffer (Ambion)

2ul 10x T7 enzyme mix (Ambion)

[275] Final volume of total reaction is 20ul. Incubate 6 hours at 37C in a PCR machine.

RNeasy clean-up of IVT product

[276] Follow previous instructions for RNeasy columns or refer to Qiagen's RNeasy protocol handbook.

[277] cRNA will most likely need to be ethanol precipitated. Resuspend in a volume compatible with the fragmentation step.

Fragmentation

[278] 15 ug of labeled RNA is usually fragmented. Try to minimize the fragmentation reaction volume; a 10 ul volume is recommended but 20 ul is all right. Do not go higher than 20 ul because the magnesium in the fragmentation buffer contributes to precipitation in the hybridization buffer.

[279] Fragment RNA by incubation at 94 C for 35 minutes in 1 x Fragmentation buffer.

5 x Fragmentation buffer:

200 mM Tris-acetate, pH 8.1

500 mM KOAc

150 mM MgOAc

[280] The labeled RNA transcript can be analyzed before and after fragmentation. Samples can be heated to 65C for 15 minutes and electrophoresed on 1% agarose/TBE gels to get an approximate idea of the transcript size range

Hybridization

[281] 200 ul (10ug cRNA) of a hybridization mix is put on the chip. If multiple hybridizations are to be done (such as cycling through a 5 chip set), then it is recommended that an initial hybridization mix of 300 ul or more be made.

Hybrization Mix: fragment labeled RNA (50ng/ul final conc.)

50 pM 948-b control oligo

1.5 pM BioB

5 pM BioC

25 pM BioD

100 pM CRE

0.1mg/ml herring sperm DNA

0.5mg/ml acetylated BSA

to 300 ul with 1xMES hyb. buffer

[282] The instruction manuals for the products used herein are incorporated herein in their entirety.

Labeling Protocol Provided Herein

Hybridization reaction:

Start with non-biotinylated IVT (purified by RNeasy columns)

(see example 1 for steps from tissue to IVT)

IVT antisense RNA; 4 µg: µl

Random Hexamers (1 µg/µl): 4 µl

H2O: µl

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14 µl

- Incubate 70°C, 10 min. Put on ice.

Reverse transcription:

5X First Strand (BRL) buffer:	6 µl
0.1 M DTT:	3 µl
50X dNTP mix:	0.6 µl
H2O:	2.4 µl
Cy3 or Cy5 dUTP (1mM):	3 µl
SS RT II (BRL):	1 µl
	16 µl

- Add to hybridization reaction.
- Incubate 30 min., 42°C.
- Add 1 μl SSII and let go for another hour.

Put on ice.

- 50X dNTP mix (25mM of cold dATP, dCTP, and dGTP, 10mM of dTTP: 25 μl each of 100mM dATP, dCTP, and dGTP; 10 μl of 100mM dTTP to 15 μl H2O. dNTPs from Pharmacia)

RNA degradation:

86 μl H2O

- Add 1.5 μl 1M NaOH/ 2mM EDTA, incubate at 65°C, 10 min.

10 μl 10N NaOH

4 μl 50mM EDTA

U-Con 30

500 μl TE/sample spin at 7000g for 10 min, save flow through for purification

Qiagen purification:

-suspend u-con recovered material in 500μl buffer PB

-proceed w/ normal Qiagen protocol

DNAse digest:

- Add 1 μl of 1/100 dil of DNAse/30μl Rx and incubate at 37°C for 15 min.

-5 min 95°C to denature enzyme

Sample preparation:

- Add:

Cot-1 DNA: 10 μl

50X dNTPs: 1 μl

Na pyro phosphate: 7.5 μl

10mg/ml Herring sperm DNA 1ul of 1/10 dilution

21.8 final vol.

- Dry down in speed vac.
- Resuspend in 15 μl H20.
- Add 0.38 μl 10% SDS.
- Heat 95°C, 2 min.

- Slow cool at room temp. for 20 min.

Put on slide and hybridize overnight at 64°C.

Washing after the hybridization:

3X SSC/0.03% SDS: 2 min. 37.5 ml 20X SSC+0.75ml 10% SDS in 250ml H2O

1X SSC: 5 min. 12.5 ml 20X SSC in 250ml H2O

0.2X SSC: 5 min. 2.5 ml 20X SSC in 250ml H2O

Dry slides in centrifuge, 1000 RPM, 1min.

[283] Scan using appropriate Photomultiplier tube (PMT) and fluorescent excitation and emission channels.

[284] The results are shown in Table 1 and Table 2. The lists of genes come from colorectal tumors from a variety of stages of the disease. The genes that are up regulated in the tumors (overall) were also found to be expressed at a limited amount or not at all in the body map. The body map consists of at least 28 tissue types, including Adrenal Gland, Bladder, Bone Marrow, Brain, Breast, Cervix, Colon, Diaphragm, Heart, Kidney, Liver, Lung, Lymph Node, Muscle, Pancreas, Prostate, Rectum, Salivary Gland, Skin, Small Intestine, Spinal Cord, Spleen, Stomach, Testis, Thymus, Thyroid Trachea and Uterus. As indicated, some of the Accession numbers include expression sequence tags (ESTs). Thus, in one embodiment herein, genes within an expression profile, also termed expression profile genes, include ESTs and are not necessarily full length.

[285] Table 1 shows Accession numbers for 1747 genes upregulated in colon tumor tissue. The table provides the exemplar accession numbers, Unigene ID numbers, unique Eos codes, descriptions of the genes encoded, and relative amount of expression as compared with expression in other normal body tissue.

TABLE 1. GENES INVOLVED IN COLORECTAL CANCER

PKey Primekey(unique probeset identifier)
Ex. Accn. Exemplar accession number
Probeset Eos Code number
Unigene# Unigene number

Pkey	Probeset	Ex Accn	UniG ID	UniGene Title	Ratio TumMet/Body
332264	EOS32195	N72849	Hs.115263	epiregulin	17.6
332716	EOS32647	L00058	Hs.79070	v-myc avian myelocytomatosis viral oncogene homolog	15.0
312845	EOS12776	AI911215	Hs.186555	ESTs	14.3
310257	EOS10188	AW389247	Hs.148826	ESTs	11.6
322567	EOS22498	AF155108		EST cluster (not in UniGene)	11.5
331060	EOS30991	N75081	Hs.21648	ESTs	10.3
322303	EOS22234	W07459		EST cluster (not in UniGene)	9.6
301891	EOS01822	AF131855	Hs.106127	Homo sapiens clone 25056 mRNA sequence	9.5
318524	EOS18455	AW291511	Hs.253687	ESTs	8.9
314001	EOS13932	AW168495	Hs.8750	ESTs	7.8
331183	EOS31114	T40769	Hs.8469	EST	7.3
315429	EOS15360	AW009951	Hs.206892	ESTs	7.3
303344	EOS03275	AA255977	Hs.250646	ESTs; Highly similar to ubiquitin-conjugating enzyme [M.musculus]	6.7
313625	EOS13556	AW468402	Hs.254020	ESTs	6.7
307084	EOS07015	AI160527		EST singleton (not in UniGene) with exon hit	6.1
314943	EOS14874	AI476797	Hs.184572	cell division cycle 2; G1 to S and G2 to M	6.1
303753	EOS03684	AW503733	Hs.170315	ESTs	5.7
315593	EOS15524	AW198103	Hs.158154	ESTs	5.3
313604	EOS13535	AI745325	Hs.182286	ESTs; Moderately similar to !!!! ALU SUBFAMILY SB2 WARNING ENTRY !!!! [H.sapiens]	5.1
312319	EOS12250	AA216698	Hs.180780	Homo sapiens agrin precursor mRNA; partial cds	5.1
312614	EOS12545	AI766732	Hs.201194	ESTs	4.8
323176	EOS23107	AW071648	Hs.123199	ESTs	4.8
317916	EOS17847	AI565071	Hs.159983	ESTs	4.7
301846	EOS01777	R20002	Hs.6823	ESTs; Weakly similar to intrinsic factor-B12 receptor precursor [H.sapiens]	4.6
311157	EOS11088	AI990122	Hs.196988	ESTs	4.6
332640	EOS32571	AA417152	Hs.5101	protein regulator of cytokinesis 1	4.6
311728	EOS11659	AW083000	Hs.184776	ribosomal protein L23a	4.5
313774	EOS13705	AW136836	Hs.144583	ESTs	4.5
312339	EOS12270	AA524394		EST cluster (not in UniGene)	4.4
315369	EOS15300	AA764918	Hs.256531	ESTs	4.3
303756	EOS03687	AI738488	Hs.115838	ESTs	4.3
301050	EOS00981	AW136973	Hs.144475	ESTs; Weakly similar to mitogen inducible gene mig-2 [H.sapiens]	4.3
300319	EOS00250	AW157646	Hs.153506	ESTs; Weakly similar to microtubule-actin crosslinking factor [M.musculus]	4.3
300664	EOS00595	AI444628	Hs.256809	ESTs	4.3
302655	EOS02586	AJ227892		EST cluster (not in UniGene) with exon hit	4.1
315175	EOS15106	AI025842	Hs.152530	ESTs	4.1
330786	EOS30717	D60374	Hs.258712	EST	4.1
310875	EOS10806	T47764	Hs.132917	ESTs	4.1
313425	EOS13356	AA745689	Hs.186838	ESTs; Weakly similar to similar to zinc finger 5 protein from Gallus gallus; U51640 [H.sapiens]	4.0
301804	EOS01735	AA581004		EST cluster (not in UniGene) with exon hit	4.0
332203	EOS32134	H49388	Hs.102082	EST	3.9
322968	EOS22899	AI905228		EST cluster (not in UniGene)	3.8
321524	EOS21455	N79126		EST cluster (not in UniGene)	3.8
302476	EOS02407	AF182294		EST cluster (not in UniGene) with exon hit	3.8
303295	EOS03226	AA205625	Hs.208067	ESTs	3.8
310016	EOS09947	AW449612	Hs.152475	ESTs	3.7
324871	EOS24802	AW297755	Hs.148832	ESTs	3.7
322887	EOS22818	AI986306	Hs.233460	ESTs; Weakly similar to KIAA0969 protein [H.sapiens]	3.7
313171	EOS13102	N67879	Hs.157695	ESTs	3.7
321638	EOS21569	AI356352	Hs.108932	ESTs	3.7
320445	EOS20376	R33916		EST cluster (not in UniGene)	3.6
302149	EOS02080	AI383794	Hs.152337	protein arginine N-methyltransferase 3(hnRNP methyltransferase S. cerevisiae)-like 3	3.6
316905	EOS16836	AW138241	Hs.210846	ESTs	3.6
313166	EOS13097	AI801098	Hs.151500	ESTs	3.6
323338	EOS23269	R74219	Hs.23348	S-phase kinase-associated protein 2 (p45)	3.5
311434	EOS11365	AW016607	Hs.201582	ESTs	3.5
312742	EOS12673	AI650363	Hs.116462	ESTs	3.4
323587	EOS23518	AI905527	Hs.141901	ESTs; Moderately similar to !!!! ALU SUBFAMILY SP WARNING ENTRY !!!! [H.sapiens]	3.4
317390	EOS17321	AW136551	Hs.181245	ESTs	3.4
315282	EOS15213	AI222165	Hs.144923	ESTs	3.4
318565	EOS18496	AI440137	Hs.164989	ESTs	3.4
307586	EOS07517	AI285499		EST singleton (not in UniGene) with exon hit	3.4
321052	EOS20983	AW372884	Hs.240770	nuclear cap binding protein subunit 2; 20kD	3.3
324338	EOS24269	AL138357	Hs.247514	ESTs	3.3
307517	EOS07448	AI275055	Hs.164989	ESTs	3.3
314852	EOS14783	AI903735	Hs.137527	ESTs; Weakly similar to X-linked retinopathy protein [H.sapiens]	3.3
324657	EOS24588	AW451142	Hs.255628	ESTs	3.2
314912	EOS14843	AI431345	Hs.161784	ESTs	3.2
324790	EOS24721	AI334367	Hs.159337	ESTs	3.2
315498	EOS15429	AA628539	Hs.116252	ESTs; Moderately similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	3.2
312857	EOS12788	AA772279	Hs.126914	ESTs	3.2

300762	EOS00693	AI497778	Hs.168053	ESTs	3.2
325587	EOS25518	c12_hs gi|6682462|ref| gn 1 + 126724 126967 ex 7 7 CDSI 2.44 244 3099		CH.12_hs gi|6682462	3.2
320654	EOS20585	AW263086	Hs.118112	ESTs	3.2
316715	EOS16646	AI440266	Hs.170673	ESTs	3.1
333279	EOS33210	CH22_522FG_126_1_LINK_EM:AC005500.GENSCAN.8-1		CH22_FGENES.126_1	3.1
309689	EOS09620	AW236171	Hs.181357	laminin receptor 1 (67kD; ribosomal protein SA)	3.1
323846	EOS23777	AA337621	Hs.137635	ESTs	3.1
324678	EOS24609	AI990739	Hs.236511	ESTs; Moderately similar to RNA splicing-related protein [R.norvegicus]	3.1
308362	EOS08293	AI613519		EST singleton (not in UniGene) with exon hit	3.1
308615	EOS08546	AI738593		EST singleton (not in UniGene) with exon hit	3.0
315397	EOS15328	AA218940	Hs.137516	ESTs	3.0
302236	EOS02167	AI128606	Hs.167558	zinc finger protein 161	3.0
321693	EOS21624	AA700017	Hs.173737	ras-related C3 botulinum toxin substrate 1 (rho family; small GTP binding protein Rac1)	3.0
330814	EOS30745	AA015730	Hs.247277	ESTs; Weakly similar to transformation-related protein [H.sapiens]	3.0
302977	EOS02908	AW263124		EST cluster (not in UniGene) with exon hit	3.0
327516	EOS27447	c_2_hs gi|6117815|ref| gn 6 + 199078 199216 ex 4 4 CDSI 9.15 139 1551		CH.02_hs gi|6117815	2.9
333278	EOS33209	CH22_521FG_125_2_LINK_EM:AC005500.GENSCAN.7-2		CH22_FGENES.125_2	2.9
302088	EOS02019	U77629	Hs.135639	achaete-scute complex (Drosophila) homolog-like 2	2.9
322718	EOS22649	AF150270	Hs.233322	ESTs; Weakly similar to cDNA EST EMBL:T01156 comes from this gene [C.elegans]	2.9
329154	EOS29085	c_x_hs gi|5868686|ref| gn 2 - 200851 201356 ex 1 3 CDSI 30.28 506 1812		CH.X_hs gi|5868686	2.9
315978	EOS15909	AA830893	Hs.119769	ESTs	2.9
302677	EOS02608	H63227	Hs.132880	ESTs; Highly similar to ubiquitin-conjugating enzyme [M.musculus]	2.9
315007	EOS14938	AI806583	Hs.125291	ESTs	2.9
303780	EOS03711	AI424014	Hs.243450	ESTs; Moderately similar to KIAA0456 protein [H.sapiens]	2.9
331362	EOS31293	AA417956	Hs.40782	ESTs	2.9
335815	EOS35746	CH22_3187FG_618_3_LINK_EM:AC005500.GENSCAN.510-3		CH22_FGENES.618_3	2.8
332070	EOS32001	AA598545	Hs.228138	EST	2.8
315720	EOS15651	AW291875	Hs.163900	ESTs	2.8
311913	EOS11844	AI358522	Hs.221417	ESTs	2.8
331014	EOS30945	H98597	Hs.30340	ESTs	2.8
322035	EOS21966	AL137517		EST cluster (not in UniGene)	2.8
338057	EOS37988	CH22_6558FG__LINK_EM:AC005500.GENSCAN.160-1		CH22_EM:AC005500.GENSCAN.160-1	2.8
335829	EOS35760	CH22_3202FG_620_3_LINK_EM:AC005500.GENSCAN.512-3		CH22_FGENES.620_3	2.8
312136	EOS12067	AW451469	Hs.209990	ESTs	2.8
303132	EOS03063	AI929819	Hs.193330	ESTs	2.8
317548	EOS17479	AI654187	Hs.195704	ESTs	2.8
325585	EOS25516	c12_hs gi|6682462|ref| gn 1 + 73476 73574 ex 5 7 CDSI 8.52 99 309 7		CH.12_hs gi|6682462	2.7
334631	EOS34562	CH22_1939FG_416_7_LINK_EM:AC005500.GENSCAN.277-7		CH22_FGENES.416_7	2.7
329156	EOS29087	c_x_hs gi|5868686|ref| gn 2 - 202013 202341 ex 3 3 CDSf 10.23 329 1814		CH.X_hs gi|5868686	2.7
318615	EOS18546	AI133617	Hs.191088	ESTs	2.7
300734	EOS00665	AW205197	Hs.240951	ESTs	2.7
324430	EOS24361	AA464018		EST cluster (not in UniGene)	2.7
322296	EOS22227	W76326	Hs.251937	ESTs	2.7
303842	EOS03773	AI337304	Hs.126268	ESTs; Weakly similar to similar to PDZ domain [C.elegans]	2.7
320909	EOS20840	D62269		EST cluster (not in UniGene)	2.7
325195	EOS25126	T20258	Hs.171443	ESTs; Weakly similar to actin binding protein MAYVEN [H.sapiens]	2.7
324959	EOS24890	AW367745	Hs.143137	ESTs	2.7
309997	EOS09928	AI291621	Hs.145199	ESTs	2.7
329367	EOS29298	c_x_hs gi|5868842|ref| gn 1 - 87201 87587 ex 1 4 CDSI 8.13 387 3908		CH.X_hs gi|5868842	2.7
316697	EOS16628	AW293174	Hs.252627	ESTs	2.7
313600	EOS13531	AA429564	Hs.185802	ESTs	2.7
301471	EOS01402	AA995014	Hs.129544	ESTs; Weakly similar to ORF YLL027w [S.cerevisiae]	2.6
300810	EOS00741	AI076890	Hs.186949	ESTs	2.6
319976	EOS19907	N48809	Hs.250824	ESTs	2.6
313434	EOS13365	W92070	Hs.231902	ESTs	2.6
333849	EOS33780	CH22_1118FG_290_8_LINK_EM:AC005500.GENSCAN.146-7		CH22_FGENES.290_8	2.6
330744	EOS30675	AA406142	Hs.12393	dTDP-D-glucose 4;6-dehydratase	2.6
309398	EOS09329	AW081820		EST singleton (not in UniGene) with exon hit	2.6
338727	EOS38658	CH22_7523FG__LINK_EM:AC005500.GENSCAN.500-2		CH22_EM:AC005500.GENSCAN.500-2	2.6
324620	EOS24551	AA448021		EST cluster (not in UniGene)	2.6
335755	EOS35686	CH22_3122FG_604_4_LINK_EM:AC005500.GENSCAN.493-9		CH22_FGENES.604_4	2.6
315858	EOS15789	AA737345		EST cluster (not in UniGene)	2.6
307288	EOS07219	AI205169		EST singleton (not in UniGene) with exon hit	2.5
330542	EOS30473	U23942	Hs.226213	cytochrome P450; 51 (lanosterol 14-alpha-demethylase)	2.5
335896	EOS35827	CH22_3273FG_635_4_LINK_EM:AC005500.GENSCAN.525-6		CH22_FGENES.635_4	2.5
316578	EOS16509	AA775623	Hs.211683	ESTs	2.5
329193	EOS29124	c_x_hs gi|5868716|ref| gn 3 + 168095 168181 ex 9 9 CDSI -1.11 87 2064		CH.X_hs gi|5868716	2.5
315193	EOS15124	AI241331	Hs.131765	ESTs	2.5
319478	EOS19409	R06841		EST cluster (not in UniGene)	2.5

334727	EOS34658	CH22_2038FG_424_1_LINK_EM:AC005500.GENSCAN.285-3		CH22_FGENES.424_1	2.5
328113	EOS28044	c_6_hs gi|5868024|ref| gn 2 - 80378 80491 ex 2 3 CDSi 3.89 114 3247		CH.06_hs gi|5868024	2.5
315214	EOS15145	AI915927	Hs.34771	ESTs	2.5
324718	EOS24649	AI557019	Hs.116467	ESTs	2.5
313326	EOS13257	AI088120	Hs.122329	ESTs	2.5
319480	EOS19411	R06933	Hs.184221	ESTs	2.5
317902	EOS17833	AI828602	Hs.211265	ESTs	2.5
323341	EOS23272	AL134875	Hs.192386	ESTs	2.5
336003	EOS35934	CH22_3385FG_664_4_LINK_DJ32I10.GENSCAN.5-4		CH22_FGENES.664_4	2.5
322992	EOS22923	AA142891	Hs.193165	ESTs	2.5
314911	EOS14842	AW292329	Hs.163481	ESTs	2.5
313603	EOS13534	AW468119		EST cluster (not in UniGene)	2.5
306469	EOS06400	AA983792		EST singleton (not in UniGene) with exon hit	2.5
324715	EOS24646	AI739168		EST cluster (not in UniGene)	2.5
302455	EOS02386	AA356923	Hs.240770	nuclear cap binding protein subunit 2; 20kD	2.4
321023	EOS20954	H25135	Hs.125608	ESTs	2.4
302099	EOS02030	AL021397	Hs.137576	ribosomal protein L34 pseudogene 1	2.4
314092	EOS14023	AI984040	Hs.226946	ESTs	2.4
318587	EOS18518	AA779704	Hs.168830	ESTs	2.4
303702	EOS03633	AW500748	Hs.224961	ESTs; Weakly similar to 73 kDA subunit of cleavage and polyadenylation specificity factor [H.sapiens]	2.4
301822	EOS01753	X17033	Hs.1142	integrin; alpha 2 (CD49B; alpha 2 subunit of VLA-2 receptor)	2.4
322694	EOS22625	AI110872		EST cluster (not in UniGene)	2.4
323333	EOS23264	AA228883		EST cluster (not in UniGene)	2.4
301954	EOS01885	AJ009936	Hs.118138	nuclear receptor subfamily 1; group I; member 2	2.4
331363	EOS31294	AA421562	Hs.91011	anterior gradient 2 (Xenepus laevis) homolog	2.4
303811	EOS03742	AW182340	Hs.246155	ESTs; Weakly similar to DNA TOPOISOMERASE I [H.sapiens]	2.4
308243	EOS08174	AI560037		EST singleton (not in UniGene) with exon hit	2.4
336021	EOS35952	CH22_3404FG_669_10_LINK_DJ32I10.GENSCAN.9-15		CH22_FGENES.669_10	2.4
334789	EOS34720	CH22_2101FG_432_14_LINK_EM:AC005500.GENSCAN.293-17		CH22_FGENES.432_14	2.4
320807	EOS20738	AA086110	Hs.188536	Homo sapiens clone 24838 mRNA sequence	2.4
328903	EOS28834	c_8_hs gi|5868514|ref| gn 1 + 23625 24468 ex 3 5 CDSi 91.18 844 219		CH.08_hs gi|5868514	2.4
338759	EOS38690	CH22_7581FG__LINK_EM:AC005500.GENSCAN.517-6		CH22_EM:AC005500.GENSCAN.517-6	2.3
333769	EOS33700	CH22_1036FG_271_8_LINK_EM:AC005500.GENSCAN.127-8		CH22_FGENES.271_8	2.3
303597	EOS03528	AI792141	Hs.143560	ESTs; Weakly similar to brain mitochondrial carrier protein-1 [H.sapiens]	2.3
305898	EOS05829	AA872838	Hs.242463	keratin 8	2.3
304439	EOS04370	AA398882		EST singleton (not in UniGene) with exon hit	2.3
301604	EOS01535	AA373124	Hs.105837	ESTs; Weakly similar to C17G10.1 [C.elegans]	2.3
315071	EOS15002	AA552690	Hs.152423	ESTs	2.3
330565	EOS30496	U51095	Hs.1545	caudal type homeo box transcription factor 1	2.3
331589	EOS31520	N71027	Hs.41856	ESTs	2.3
303216	EOS03147	AA581439	Hs.152328	ESTs	2.3
324988	EOS24919	T06997		EST cluster (not in UniGene)	2.3
312996	EOS12927	AA249018		EST cluster (not in UniGene)	2.3
332314	EOS32245	T25862	Hs.101774	ESTs	2.3
313325	EOS13256	AI420611	Hs.127832	ESTs	2.3
322991	EOS22922	C18965	Hs.159473	ESTs	2.3
335496	EOS35427	CH22_2848FG_571_4_LINK_EM:AC005500.GENSCAN.460-25		CH22_FGENES.571_4	2.3
315135	EOS15066	AA627561	Hs.192446	ESTs	2.3
319488	EOS19419	AW250340		EST cluster (not in UniGene)	2.3
323571	EOS23502	AA984133	Hs.153260	c-Cbl-interacting protein	2.3
322826	EOS22757	AI807883	Hs.156932	ESTs	2.3
322221	EOS22152	AI890619	Hs.179662	nucleosome assembly protein 1-like 1	2.3
312242	EOS12173	AI380207	Hs.125276	ESTs	2.3
315238	EOS15169	AA593867	Hs.170890	ESTs	2.3
315168	EOS15099	AA622130	Hs.152524	ESTs	2.3
300504	EOS00435	AW204624	Hs.192927	ESTs; Weakly similar to Lim kinase [H.sapiens]	2.3
323243	EOS23174	W44372		EST cluster (not in UniGene)	2.3
331628	EOS31559	R80965	Hs.204079	ESTs	2.3
320746	EOS20677	AA128302		EST cluster (not in UniGene)	2.3
324598	EOS24529	AA502659	Hs.163986	ESTs	2.3
308667	EOS08598	AI758754		EST singleton (not in UniGene) with exon hit	2.2
302944	EOS02875	AA340708	Hs.256204	ESTs; Weakly similar to cyclic nucleotide-gated channel beta subunit [R.norvegicus]	2.2
316291	EOS16222	AW375974	Hs.156704	ESTs	2.2
315296	EOS15227	AA876905	Hs.125286	ESTs	2.2
334150	EOS34081	CH22_1429FG_339_1_LINK_EM:AC005500.GENSCAN.189-1		CH22_FGENES.339_1	2.2
331380	EOS31311	AA453266	Hs.246131	ESTs	2.2
321795	EOS21726	AI796896	Hs.222446	ESTs	2.2
331493	EOS31424	N34357	Hs.44571	ESTs	2.2
312890	EOS12821	AI813654	Hs.127478	ESTs	2.2
315583	EOS15514	AW003622	Hs.126555	ESTs	2.2
314306	EOS14237	AI697901	Hs.192425	ESTs	2.2
314138	EOS14069	AA740616		EST cluster (not in UniGene)	2.2
302656	EOS02587	AW293005	Hs.220905	ESTs	2.2
313564	EOS13495	AA810141	Hs.192182	ESTs	2.2
332792	EOS32723	CH22_8FG_3_2_LINK_C4G1.GENSCAN.3-2		CH22_FGENES.3_2	2.2

332020	EOS31951	AA488895	Hs.105219	ESTs	2.2
315143	EOS15074	AA878324	Hs.192734	ESTs	2.2
313385	EOS13316	AI032087	Hs.176711	ESTs	2.2
323835	EOS23766	AL042005		EST cluster (not in UniGene)	2.2
314014	EOS13945	AW291847	Hs.121715	ESTs; Weakly similar to HP protein [H.sapiens]	2.2
336016	EOS35947	CH22_3399FG_669_5_LINK_DJ32I10.GENSCAN.9-10		CH22_FGENES.669_5	2.2
323218	EOS23149	AF131846	Hs.13396	Homo sapiens clone 25028 mRNA sequence	2.2
338059	EOS37990	CH22_6561FG__LINK_EM:AC005500.GENSCAN.160-4		CH22_EM:AC005500.GENSCAN.160-4	2.2
302613	EOS02544	AA371059	Hs.251636	ubiquitin specific protease 3	2.2
304852	EOS04783	AA588595		EST singleton (not in UniGene) with exon hit	2.2
308457	EOS08388	AI669859		EST singleton (not in UniGene) with exon hit	2.2
311736	EOS11667	AA765897		EST cluster (not in UniGene)	2.2
334183	EOS34114	CH22_1464FG_350_13_LINK_EM:AC005500.GENSCAN.209-16		CH22_FGENES.350_13	2.2
315021	EOS14952	AA533447		EST cluster (not in UniGene)	2.2
303013	EOS02944	F07898	Hs.214190	interleukin enhancer binding factor 1	2.2
315006	EOS14937	AI538613	Hs.135657	ESTs	2.2
337534	EOS37465	CH22_5803FG_828_3_		CH22_FGENES.828-3	2.2
303276	EOS03207	AA431599	Hs.132799	ESTs	2.1
318617	EOS18548	AW247252	Hs.75514	nucleoside phosphorylase	2.1
330760	EOS30691	AA448663	Hs.30469	ESTs	2.1
319545	EOS19476	R83716	Hs.14355	ESTs	2.1
312252	EOS12183	AI128388	Hs.143655	ESTs	2.1
322882	EOS22813	AW248508	Hs.2491	DiGeorge syndrome critical region gene 2	2.1
312684	EOS12615	AW294020	Hs.117721	ESTs	2.1
315782	EOS15713	AW515455	Hs.115558	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	2.1
320076	EOS20007	AI653733	Hs.204079	ESTs	2.1
300566	EOS00497	H86709	Hs.21371	son of sevenless (Drosophila) homolog 1	2.1
300908	EOS00839	AA618335	Hs.146137	ESTs; Weakly similar to putative [C.elegans]	2.1
314778	EOS14709	AW079559	Hs.152258	ESTs	2.1
319233	EOS19164	R21054	Hs.211522	ESTs	2.1
335488	EOS35419	CH22_2840FG_570_20_LINK_EM:AC005500.GENSCAN.460-15		CH22_FGENES.570_20	2.1
334616	EOS34547	CH22_1923FG_411_15_LINK_EM:AC005500.GENSCAN.274-22		CH22_FGENES.411_15	2.1
306792	EOS06723	AI042426		EST singleton (not in UniGene) with exon hit	2.1
301661	EOS01592	AI815558		EST cluster (not in UniGene) with exon hit	2.1
311332	EOS11263	AW292247	Hs.255052	ESTs	2.1
314785	EOS14716	AI538226	Hs.135184	ESTs	2.1
301460	EOS01391	AW196758	Hs.165998	DKFZP564M2423 protein	2.1
332015	EOS31946	AA487910	Hs.208800	ESTs; Weakly similar to !!!! ALU CLASS B WARNING ENTRY !!!! [H.sapiens]	2.1
321529	EOS21460	AI269506	Hs.146066	ESTs	2.1
323740	EOS23671	AA324643	Hs.246106	ESTs	2.1
336019	EOS35950	CH22_3402FG_669_8_LINK_DJ32I10.GENSCAN.9-13		CH22_FGENES.669_8	2.1
314954	EOS14885	AA521381	Hs.187726	ESTs	2.1
303037	EOS02968	AF118395		EST cluster (not in UniGene) with exon hit	2.1
302056	EOS01987	AI457532	Hs.126082	ESTs; Moderately similar to ROSA26AS [M.musculus]	2.1
315178	EOS15109	AW362945	Hs.162459	ESTs	2.1
332246	EOS32177	N57927	Hs.120777	ESTs; Weakly similar to RNA POLYMERASE II ELONGATION FACTOR ELL2 [H.sapiens]	2.0
334288	EOS34219	CH22_1577FG_369_18_LINK_EM:AC005500.GENSCAN.229-18		CH22_FGENES.369_18	2.0
324690	EOS24621	N88286	Hs.132808	ESTs; Weakly similar to Similar to S.pombe -rad4+/cut5+product [H.sapiens]	2.0
305257	EOS05188	AA679005		EST singleton (not in UniGene) with exon hit	2.0
311315	EOS11246	AW450536	Hs.209260	ESTs	2.0
311988	EOS11919	AW016096	Hs.13801	ESTs	2.0
302638	EOS02569	AA463798	Hs.102696	ESTs; Weakly similar to C11D2.4 [C.elegans]	2.0
320531	EOS20462	W03691	Hs.24884	ESTs; Moderately similar to RNA polymerase I associated factor [M.musculus]	2.0
323604	EOS23535	AI751438	Hs.182827	ESTs; Weakly similar to !!!! ALU SUBFAMILY SQ WARNING ENTRY !!!! [H.sapiens]	2.0
308852	EOS08783	AI829848	Hs.182937	peptidylprolyl isomerase A (cyclophilin A)	2.0
320521	EOS20452	N31464	Hs.24743	ESTs	2.0
331306	EOS31237	AA252079	Hs.63931	dachshund (Drosophila) homolog	2.0
314941	EOS14872	AA515902	Hs.130650	ESTs	2.0
336684	EOS36615	CH22_4167FG_46_1_		CH22_FGENES.46-1	2.0
301137	EOS01068	AF049569	Hs.137096	ESTs	2.0
338454	EOS38385	CH22_7128FG__LINK_EM:AC005500.GENSCAN.360-4		CH22_EM:AC005500.GENSCAN.360-4	2.0
309700	EOS09631	AW241170	Hs.179661	Homo sapiens clone 24703 beta-tubulin mRNA; complete cds	2.0
330262	EOS30193	c_5_p2 gi|6671884|gb|A gn 1 + 67913 68053 ex 3 3 CDSI 5.41 141 597		CH.05_p2 gi|6671884	2.0
324163	EOS24094	AL046827	Hs.134651	ESTs	2.0
316493	EOS16424	AA766142	Hs.131810	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	2.0
311873	EOS11804	AA730045	Hs.187866	ESTs	2.0
326757	EOS26688	c20_hs gi|6249610|ref| gn 3 + 74531 74597 ex 1 3 CDSf 9.52 67 1416		CH.20_hs gi|6249610	2.0
319167	EOS19098	F05984	Hs.250138	protein phosphatase 2C; magnesium-dependent; catalytic subunit	2.0
316011	EOS15942	AW516953	Hs.201372	ESTs	2.0
313635	EOS13566	AA507227	Hs.6390	ESTs	2.0
310027	EOS09958	AW449009	Hs.126647	ESTs	2.0
336662	EOS36593	CH22_4138FG_41_1_		CH22_FGENES.41-1	2.0
334648	EOS34579	CH22_1956FG_417_15_LINK_EM:AC005500.GENSCAN.278-15		CH22_FGENES.417_15	2.0
308676	EOS08607	AI761036		EST singleton (not in UniGene) with exon hit	2.0
312047	EOS11978	AA588275	Hs.14258	ESTs	2.0

324826	EOS24757	AA704806	Hs.143842	ESTs	2.0
322889	EOS22820	AA081924	Hs.211417	ESTs	2.0
316345	EOS16276	AW139408	Hs.152940	ESTs	2.0
313922	EOS13853	AI702038	Hs.100057	ESTs	2.0
319423	EOS19354	T83024	Hs.15119	ESTs	2.0
320244	EOS20175	AA296922	Hs.129778	gastrointestinal peptide	2.0
308957	EOS08888	AI869642		EST singleton (not in UniGene) with exon hit	2.0
334223	EOS34154	CH22_1507FG_360_4_LINK_EM:AC005500.GENSCAN.218-4		CH22_FGENES.360_4	1.9
302980	EOS02911	W93435		EST cluster (not in UniGene) with exon hit	1.9
312153	EOS12084	AA759250	Hs.153028	cytochrome b-561	1.9
326460	EOS26391	c19_hs gi|5867400|ref| gn 3 - 142633 142935 ex 1 2 CDSI 19.03 303 1731		CH.19_hs gi|5867400	1.9
319962	EOS19893	H06350	Hs.135056	ESTs	1.9
307064	EOS06995	AI149335		EST singleton (not in UniGene) with exon hit	1.9
331608	EOS31539	N89861	Hs.44162	ESTs; Weakly similar to cDNA EST yk342h12.5 comes from this gene [C.elegans]	1.9
328142	EOS28073	c_6_hs gi|5868050|ref| gn 1 - 9656 9778 ex 2 6 CDSi 11.11 123 3339		CH.06_hs gi|5868050	1.9
312527	EOS12458	AI695522	Hs.191271	ESTs	1.9
318581	EOS18512	AA769058		EST cluster (not in UniGene)	1.9
319979	EOS19910	AB018281	Hs.107479	KIAA0738 gene product	1.9
336107	EOS36038	CH22_3496FG_696_3_LINK_DA59H18.GENSCAN.4-3		CH22_FGENES.696_3	1.9
305232	EOS05163	AA670052	Hs.195188	glyceraldehyde-3-phosphate dehydrogenase	1.9
315043	EOS14974	AA806538	Hs.130732	ESTs	1.9
323377	EOS23308	AA133260	Hs.8454	protein kinase; cAMP-dependent; regulatory; type II; alpha	1.9
338260	EOS38191	CH22_6863FG__LINK_EM:AC005500.GENSCAN.279-10		CH22_EM:AC005500.GENSCAN.279-10	1.9
334891	EOS34822	CH22_2208FG_452_5_LINK_EM:AC005500.GENSCAN.341-8		CH22_FGENES.452_5	1.9
316055	EOS15986	AA693880		EST cluster (not in UniGene)	1.9
312414	EOS12345	AI915014	Hs.164235	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.9
300225	EOS00156	AI989963	Hs.197505	ESTs	1.9
332607	EOS32538	R41791	Hs.36566	LIM domain kinase 1	1.9
312405	EOS12336	AI523875		EST cluster (not in UniGene)	1.9
313605	EOS13536	AI761786	Hs.204674	ESTs	1.9
337755	EOS37686	CH22_6105FG__LINK_EM:AC000097.GENSCAN.109-2		CH22_EM:AC000097.GENSCAN.109-2	1.9
323216	EOS23147	AA332145		EST cluster (not in UniGene)	1.9
334872	EOS34803	CH22_2186FG_450_2_LINK_EM:AC005500.GENSCAN.339-2		CH22_FGENES.450_2	1.9
332034	EOS31965	AA489847	Hs.112019	ESTs; Moderately similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.9
332103	EOS32034	AA609161	Hs.112657	ESTs; Weakly similar to ORF YOR243c [S.cerevisiae]	1.9
318196	EOS18127	AI056776	Hs.133397	ESTs	1.9
329141	EOS29072	c_x_hs gi|6017060|ref| gn 1 + 343924 343997 ex 2 3 CDSI 8.53 74 1715		CH.X_hs gi|6017060	1.9
321539	EOS21470	N98619	Hs.62461	ARP2 (actin-related protein 2; yeast) homolog	1.9
313881	EOS13812	AA535580	Hs.16331	ESTs	1.9
314046	EOS13977	AW021917	Hs.181878	ESTs	1.9
336045	EOS35976	CH22_3430FG_679_7_LINK_DJ32I10.GENSCAN.18-8		CH22_FGENES.679_7	1.9
324799	EOS24730	AW272262	Hs.250468	ESTs	1.9
312656	EOS12587	AW152449	Hs.226469	ESTs	1.9
324662	EOS24593	AW504689		EST cluster (not in UniGene)	1.9
323930	EOS23861	AA570698	Hs.193203	ESTs	1.9
314465	EOS14396	AA602917	Hs.156974	ESTs	1.9
335897	EOS35828	CH22_3274FG_635_5_LINK_EM:AC005500.GENSCAN.525-7		CH22_FGENES.635_5	1.9
321746	EOS21677	AI806500	Hs.102652	ESTs; Weakly similar to KIAA0437 [H.sapiens]	1.9
335687	EOS35618	CH22_3048FG_596_2_LINK_EM:AC005500.GENSCAN.488-2		CH22_FGENES.596_2	1.9
330731	EOS30662	AA278816	Hs.177204	ESTs	1.9
315542	EOS15473	AA079476	Hs.109857	ESTs; Highly similar to CGI-89 protein [H.sapiens]	1.9
336379	EOS36310	CH22_3791FG_821_7_LINK_BA232E17.GENSCAN.4-19		CH22_FGENES.821_7	1.9
305691	EOS05622	AA813590	Hs.119500	karyopherin alpha 4 (importin alpha 3)	1.9
310639	EOS10570	AW269082	Hs.175162	ESTs	1.9
327481	EOS27412	c_2_hs gi|5867783|ref| gn 3 + 104472 104673 ex 1 4 CDSf 14.33 202 1308		CH.02_hs gi|5867783	1.9
301910	EOS01841	T84852	Hs.98370	cytochrome P540 family member predicted from ESTs	1.9
335478	EOS35409	CH22_2830FG_569_1_LINK_EM:AC005500.GENSCAN.456-1		CH22_FGENES.569_1	1.9
331135	EOS31066	R61398	Hs.4197	ESTs	1.9
335690	EOS35621	CH22_3051FG_596_5_LINK_EM:AC005500.GENSCAN.488-5		CH22_FGENES.596_5	1.9
308047	EOS07978	AI459633		EST singleton (not in UniGene) with exon hit	1.9
334500	EOS34431	CH22_1800FG_397_16_LINK_EM:AC005500.GENSCAN.260-18		CH22_FGENES.397_16	1.9
338250	EOS38181	CH22_6848FG__LINK_EM:AC005500.GENSCAN.269- 2		CH22_EM:AC005500.GENSCAN.269-2	1.8
320618	EOS20549	AI220276	Hs.235228	EST	1.8
335044	EOS34975	CH22_2367FG_480_1_LINK_EM:AC005500.GENSCAN.374-1		CH22_FGENES.480_1	1.8
313789	EOS13720	AI167810	Hs.217743	ESTs	1.8
311911	EOS11842	AI087123	Hs.114434	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.8
320180	EOS20111	AA846203	Hs.193974	ESTs; Weakly similar to alternatively spliced product using exon 13A [H.sapiens]	1.8

311036	EOS10967	AI539227	Hs.214039	ESTs	1.8
323903	EOS23834	AA773580	Hs.193598	ESTs	1.8
318676	EOS18607	T57448	Hs.15467	ESTs; Moderately similar to putative phosphoinositide 5-phosphatase type II [M.musculus]	1.8
303007	EOS02938	AA478876	Hs.7037	pallid (mouse) homolog; pallidin	1.8
334806	EOS34737	CH22_2119FG_435_7_LINK_EM:AC005500.GENSCAN.296-6		CH22_FGENES.435_7	1.8
311767	EOS11698	AI076686	Hs.190066	ESTs	1.8
331750	EOS31681	AA284372	Hs.111471	ESTs	1.8
314872	EOS14803	AI144254	Hs.239726	ESTs	1.8
314071	EOS14002	AA192455	Hs.188690	ESTs	1.8
328450	EOS28381	c_7_hs gi|5868425|ref| gn 2 - 209192 209321 ex 2 3 CDSI 10.41 130 1407		CH.07_hs gi|5868425	1.8
328857	EOS28788	c_7_hs gi|6381927|ref| gn 3 - 80557 81051 ex 1 1 CDSo 41.51 495 6090		CH.07_hs gi|6381927	1.8
313781	EOS13712	AA078836		EST cluster (not in UniGene)	1.8
336953	EOS36884	CH22_4746FG_361_22_		CH22_FGENES.361-22	1.8
300233	EOS00164	AI380777	Hs.189402	ESTs	1.8
326862	EOS26793	c20_hs gi|6552465|ref| gn 2 + 107702 107782 ex 12 13 CDSi 3.62 81 2149		CH.20_hs gi|6552465	1.8
312364	EOS12295	R40111	Hs.187618	ESTs	1.8
321541	EOS21472	AI220292	Hs.254467	ESTs	1.8
307432	EOS07363	AI244259	Hs.181165	eukaryotic translation elongation factor 1 alpha 1	1.8
320921	EOS20852	R94038	Hs.199538	inhibin; beta C	1.8
333110	EOS33041	CH22_338FG_79_16_LINK_EM:AC000097.GENSCAN.59-15		CH22_FGENES.79_16	1.8
324914	EOS24845	AA847510	Hs.161292	ESTs	1.8
312681	EOS12612	AI028149	Hs.193124	pyruvate dehydrogenase kinase; isoenzyme 3	1.8
335697	EOS35628	CH22_3058FG_596_12_LINK_EM:AC005500.GENSCAN.488-13		CH22_FGENES.596_12	1.8
308462	EOS08393	AI671311		EST singleton (not in UniGene) with exon hit	1.8
312138	EOS12069	T89405	Hs.218851	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.8
309116	EOS09047	AI927149	Hs.29797	ribosomal protein L10	1.8
320730	EOS20661	AA534539	Hs.151072	ESTs	1.8
300844	EOS00775	AL042759	Hs.191762	ESTs	1.8
337570	EOS37501	CH22_5856FG__LINK_C65E1.GENSCAN.4-2		CH22_C65E1.GENSCAN.4-2	1.8
332756	EOS32687	D63479	Hs.115907	diacylglycerol kinase; delta (130kD)	1.8
332161	EOS32092	AA621523	Hs.165464	ESTs	1.8
300942	EOS00873	AW275006	Hs.195969	ESTs	1.8
300680	EOS00611	AW468066	Hs.257712	ESTs; Weakly similar to KIAA0986 protein [H.sapiens]	1.8
328783	EOS28714	c_7_hs gi|5868309|ref| gn 5 - 73658 73822 ex 2 5 CDSI 0.78 165 5371		CH.07_hs gi|5868309	1.8
307542	EOS07473	AI280859		EST singleton (not in UniGene) with exon hit	1.8
331975	EOS31906	AA464972	Hs.99624	ESTs	1.8
321532	EOS21463	T77886	Hs.83428	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 (p105)	1.8
318721	EOS18652	Z28504		EST cluster (not in UniGene)	1.8
302124	EOS02055	AB023967	Hs.145078	regulator of differentiation (in S. pombe) 1	1.8
323541	EOS23472	AI185116	Hs.104613	ESTs; Weakly similar to Similar to S.cerevisiae hypothetical protein L3111 [H.sapiens]	1.8
331057	EOS30988	N71399	Hs.28143	ESTs	1.8
316860	EOS16791	AW139099	Hs.127489	ESTs	1.8
330601	EOS30532	U90916	Hs.82845	Human clone 23815 mRNA sequence	1.8
307334	EOS07265	AI214811	Hs.220615	ESTs; Weakly similar to TFII-I protein [H.sapiens]	1.8
323195	EOS23126	AI064982	Hs.117950	multifunctional polypeptide similar to SAICAR synthetase and AIR carboxylase	1.8
303856	EOS03787	AA968589	Hs.944	glucose phosphate isomerase	1.8
321553	EOS21484	H92449	Hs.116406	ESTs	1.8
332705	EOS32636	T59161	Hs.76293	thymosin; beta 10	1.8
333139	EOS33070	CH22_368FG_83_16_LINK_EM:AC000097.GENSCAN.67-19		CH22_FGENES.83_16	1.8
338997	EOS38928	CH22_7881FG__LINK_DA59H18.GENSCAN.8-22		CH22_DA59H18.GENSCAN.8-22	1.8
301509	EOS01440	AI025435	Hs.117532	ESTs	1.8
314522	EOS14453	AI732331	Hs.187750	ESTs; Moderately similar to !!!! ALU CLASS C WARNING ENTRY !!!! [H.sapiens]	1.8
303072	EOS03003	AF157833		EST cluster (not in UniGene) with exon hit	1.8
305271	EOS05202	AA679895		EST singleton (not in UniGene) with exon hit	1.8
335287	EOS35218	CH22_2629FG_526_11_LINK_EM:AC005500.GENSCAN.420-4		CH22_FGENES.526_11	1.8
321286	EOS21217	AI380940		EST cluster (not in UniGene)	1.8
318740	EOS18671	NM_002543		EST cluster (not in UniGene)	1.8
323465	EOS23396	AA287406		EST cluster (not in UniGene)	1.8
300611	EOS00542	N75450		EST cluster (not in UniGene) with exon hit	1.8
306235	EOS06166	AA932299		EST singleton (not in UniGene) with exon hit	1.8
336721	EOS36652	CH22_4244FG_83_17_		CH22_FGENES.83-17	1.8
311291	EOS11222	AA782601	Hs.122684	ESTs	1.8
310247	EOS10178	AI224982	Hs.211454	ESTs	1.8
316564	EOS16495	AI743571	Hs.168799	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.8
328170	EOS28101	c_6_hs gi|5868071|ref| gn 1 + 93170 93295 ex 9 9 CDSI 13.31 126 3591		CH.06_hs gi|5868071	1.8
300909	EOS00840	AW295479	Hs.154903	ESTs; Weakly similar to Abl substrate ena [D.melanogaster]	1.8
330869	EOS30800	AA115197	Hs.183702	ESTs	1.8
311048	EOS10979	AA506952	Hs.210508	ESTs	1.8
333764	EOS33695	CH22_1031FG_271_3_LINK_EM:AC005500.GENSCAN.127-3		CH22_FGENES.271_3	1.8
338862	EOS38793	CH22_7715FG__LINK_DJ32I10.GENSCAN.1-6		CH22_DJ32I10.GENSCAN.1-6	1.8
331467	EOS31398	N22206	Hs.43112	ESTs	1.8
327742	EOS27673	c_5_hs gi|5867944|ref| gn 3 - 143307 143512 ex 1 3 CDSI 11.07 206 172			

				CH.05_hs gi|5867944	1.8
320955	EOS20886	AL049415	Hs.204290	Homo sapiens mRNA; cDNA DKFZp586N2119 (from clone DKFZp586N2119)	1.8
323589	EOS23520	AW390054	Hs.192843	ESTs	1.8
319951	EOS19882	AA307665	Hs.14559	ESTs	1.8
333763	EOS33694	CH22_1030FG_271_2_LINK_EM:AC005500.GENSCAN.127-2		CH22_FGENES.271_2	1.7
331046	EOS30977	N66563	Hs.191358	ESTs	1.7
320001	EOS19932	AA873350		EST cluster (not in UniGene)	1.7
316869	EOS16800	AI954880	Hs.134604	ESTs	1.7
310774	EOS10705	AW134483	Hs.164371	ESTs	1.7
319379	EOS19310	T91443	Hs.193963	ESTs	1.7
321549	EOS21480	AA470984	Hs.161947	ESTs	1.7
300823	EOS00754	AI863068	Hs.222665	ESTs; Weakly similar to putative zinc finger protein NY-REN-34 antigen [H.sapiens]	1.7
324228	EOS24159	AI798146	Hs.207780	ESTs	1.7
313902	EOS13833	AI308165	Hs.156242	ESTs	1.7
308928	EOS08859	AI863908		EST singleton (not in UniGene) with exon hit	1.7
333770	EOS33701	CH22_1037FG_272_1_LINK_EM:AC005500.GENSCAN.127-10		CH22_FGENES.272_1	1.7
316934	EOS16865	AI571647	Hs.146170	ESTs	1.7
313219	EOS13150	N74924	Hs.182099	ESTs	1.7
317360	EOS17291	AI125252	Hs.126419	ESTs	1.7
303530	EOS03461	AI274851	Hs.258744	ESTs	1.7
334739	EOS34670	CH22_2051FG_424_14_LINK_EM:AC005500.GENSCAN.285-16		CH22_FGENES.424_14	1.7
337670	EOS37601	CH22_5996FG__LINK_EM:AC000097.GENSCAN.57-2		CH22_EM:AC000097.GENSCAN.57-2	1.7
312079	EOS12010	T79745	Hs.189717	ESTs	1.7
320211	EOS20142	AL039402	Hs.125783	DEME-6 protein	1.7
316218	EOS16149	AW207642	Hs.174021	ESTs	1.7
335682	EOS35613	CH22_3043FG_595_2_LINK_EM:AC005500.GENSCAN.487-11		CH22_FGENES.595_2	1.7
330696	EOS30627	AA022632	Hs.15825	ESTs	1.7
314449	EOS14380	AL042667	Hs.225539	ESTs	1.7
311972	EOS11903	N51511	Hs.188449	ESTs	1.7
307691	EOS07622	AI318285	Hs.182371	prothymosin; alpha (gene sequence 28)	1.7
338249	EOS38180	CH22_6847FG__LINK_EM:AC005500.GENSCAN.269-1		CH22_EM:AC005500.GENSCAN.269-1	1.7
326399	EOS26330	c19_hs gi|5867353|ref| gn 1 + 6385 6536 ex 6 6 CDSl 10.69 152 684		CH.19_hs gi|5867353	1.7
313290	EOS13221	AI753247	Hs.206454	ESTs	1.7
301615	EOS01546	W39477		EST cluster (not in UniGene) with exon hit	1.7
307034	EOS06965	AI142526		EST singleton (not in UniGene) with exon hit	1.7
313577	EOS13508	AA565051	Hs.155029	ESTs	1.7
324703	EOS24634	AB009282	Hs.31086	Homo sapiens mRNA for cytochrome b5; partial cds	1.7
321317	EOS21248	AI937060	Hs.202040	ESTs; Weakly similar to KIAA0938 protein [H.sapiens]	1.7
312278	EOS12209	AW205234	Hs.201587	ESTs	1.7
333358	EOS33289	CH22_604FG_141_9_LINK_EM:AC005500.GENSCAN.21-9		CH22_FGENES.141_9	1.7
322735	EOS22666	AA086123		EST cluster (not in UniGene)	1.7
326752	EOS26683	c20_hs gi|5867615|ref| gn 1 - 1214 1562 ex 2 2 CDSf 33.07 349 1366		CH.20_hs gi|5867615	1.7
314733	EOS14664	AW452355	Hs.256037	ESTs	1.7
312902	EOS12833	AW292797	Hs.130316	ESTs	1.7
322653	EOS22584	AI828854	Hs.171891	ESTs	1.7
336015	EOS35946	CH22_3398FG_669_4_LINK_DJ32I10.GENSCAN.9-9		CH22_FGENES.669_4	1.7
324500	EOS24431	AW269819	Hs.169905	ESTs	1.7
310900	EOS10831	AI922728	Hs.165803	ESTs; Weakly similar to !!!! ALU SUBFAMILY SB WARNING ENTRY !!!! [H.sapiens]	1.7
337908	EOS37839	CH22_6323FG__LINK_EM:AC005500.GENSCAN.57-1		CH22_EM:AC005500.GENSCAN.57-1	1.7
304084	EOS04015	T91986		EST singleton (not in UniGene) with exon hit	1.7
332539	EOS32470	AA412528	Hs.20183	ESTs; Weakly similar to cDNA EST EMBL:T01421 comes from this gene [C.elegans]	1.7
314332	EOS14263	AL037551	Hs.95612	ESTs	1.7
321412	EOS21343	AW366305		EST cluster (not in UniGene)	1.7
312187	EOS12118	AA700439	Hs.188490	ESTs	1.7
314147	EOS14078	AI656135	Hs.129805	ESTs	1.7
303131	EOS03062	AW081061	Hs.103180	actin-like 6	1.7
331341	EOS31272	AA303125	Hs.119009	ESTs; Weakly similar to !!!! ALU SUBFAMILY SB2 WARNING ENTRY !!!! [H.sapiens]	1.7
313615	EOS13546	AW295194	Hs.25264	DKFZP434N126 protein	1.7
329598	EOS29529	c10_p2 gi|3962482|gb|A gn 4 + 39924 40220 ex 2 3 CDSl 8.71 297 420		CH.10_p2 gi|3962482	1.7
303579	EOS03510	AA381124	Hs.193353	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.7
331692	EOS31623	W93592	Hs.47343	ESTs	1.7
323977	EOS23908	AW328177	Hs.234713	ESTs	1.7
332930	EOS32861	CH22_151FG_38_4_LINK_C20H12.GENSCAN.29-4		CH22_FGENES.38_4	1.7
326596	EOS26527	c19_hs gi|6138928|ref| gn 4 + 133386 133563 ex 7 9 CDSl -1.32 178 3520		CH.19_hs gi|6138928	1.7
314946	EOS14877	AI097229	Hs.217484	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.7
315357	EOS15288	AA608684	Hs.121705	ESTs; Moderately similar to !!!! ALU CLASS C WARNING ENTRY !!!! [H.sapiens]	1.7
324728	EOS24659	AA303024		EST cluster (not in UniGene)	1.7
317501	EOS17432	AA931245	Hs.137097	ESTs	1.7
332219	EOS32150	N22508	Hs.139315	ESTs	1.7
335369	EOS35300	CH22_2718FG_543_7_LINK_EM:AC005500.GENSCAN.432-9		CH22_FGENES.543_7	1.7
322417	EOS22348	W36286	Hs.171873	ESTs; Weakly similar to PUTATIVE STEROID DEHYDROGENASE KIK-I [M.musculus]	1.7

316100	EOS16031	AW203986	Hs.213003	ESTs	1.7
314866	EOS14797	AW305124	Hs.191682	ESTs	1.7
300328	EOS00259	AW015860	Hs.224623	ESTs	1.7
315676	EOS15607	AW002565	Hs.136590	ESTs	1.7
314183	EOS14114	AA748600		EST cluster (not in UniGene)	1.7
321354	EOS21285	AA078493		EST cluster (not in UniGene)	1.7
311904	EOS11835	T86907	Hs.119371	ESTs	1.7
322890	EOS22821	AA082030		EST cluster (not in UniGene)	1.7
302759	EOS02690	AI885815	Hs.184727	ESTs	1.7
324600	EOS24531	AA503297	Hs.117108	ESTs	1.7
314973	EOS14904	AW273128	Hs.254669	EST	1.7
324432	EOS24363	AA464510		EST cluster (not in UniGene)	1.7
331520	EOS31451	N49068	Hs.93966	ESTs	1.7
308380	EOS08311	AI623988		EST singleton (not in UniGene) with exon hit	1.7
331010	EOS30941	H95039	Hs.32168	KIAA0442 protein	1.7
325363	EOS25294	c12_hs gi|5866920|ref| gn 7 + 700446 700516 ex 6 8 CDSi -6.58 71 113		CH.12_hs gi|5866920	1.7
310470	EOS10401	AI281848	Hs.165547	ESTs	1.7
330711	EOS30642	AA164687	Hs.177576	mannosyl (alpha-1;3-)-glycoprotein beta-1;4-N-acetylglucosaminyltransferase; isoenzyme A	1.7
332074	EOS32005	AA599012	Hs.22826	ESTs	1.7
309732	EOS09663	AW262211	Hs.5662	guanine nucleotide binding protein (G protein); beta polypeptide 2-like 1	1.6
306337	EOS06268	AA954221	Hs.73742	ribosomal protein; large; P0	1.6
335189	EOS35120	CH22_2525FG_507_4_LINK_EM:AC005500.GENSCAN.400-4		CH22_FGENES.507_4	1.6
316253	EOS16184	AI919537	Hs.118056	ESTs	1.6
332908	EOS32839	CH22_129FG_36_12_LINK_C20H12.GENSCAN.28-9		CH22_FGENES.36_12	1.6
310002	EOS09933	AI439096	Hs.25832	ESTs	1.6
332258	EOS32189	N68670	Hs.103808	ESTs; Weakly similar to RanBPM [H.sapiens]	1.6
336182	EOS36113	CH22_3576FG_715_2_LINK_DA59H18.GENSCAN.19-3		CH22_FGENES.715_2	1.6
328987	EOS28918	c_9_hs gi|5868535|ref| gn 1 - 25705 25764 ex 3 10 CDSi 9.90 60 438		CH.09_hs gi|5868535	1.6
324481	EOS24412	AI916284	Hs.199671	ESTs	1.6
331406	EOS31337	AA610064	Hs.23440	KIAA1105 protein	1.6
332280	EOS32211	R38100	Hs.106294	ESTs	1.6
332173	EOS32104	F09281	Hs.90424	ESTs	1.6
335739	EOS35670	CH22_3102FG_601_10_LINK_EM:AC005500.GENSCAN.491-10		CH22_FGENES.601_10	1.6
332104	EOS32035	AA609177	Hs.109363	ESTs	1.6
315033	EOS14964	AI493046	Hs.146133	ESTs	1.6
334740	EOS34671	CH22_2052FG_424_15_LINK_EM:AC005500.GENSCAN.285-17		CH22_FGENES.424_15	1.6
334783	EOS34714	CH22_2095FG_432_8_LINK_EM:AC005500.GENSCAN.293-11		CH22_FGENES.432_8	1.6
308010	EOS07941	AI439190	Hs.181165	eukaryotic translation elongation factor 1 alpha 1	1.6
304521	EOS04452	AA464716		EST singleton (not in UniGene) with exon hit	1.6
318719	EOS18650	Z25900	Hs.18724	Homo sapiens mRNA; cDNA DKFZp564F093 (from clone DKFZp564F093)	1.6
321920	EOS21851	N63915		EST cluster (not in UniGene)	1.6
315019	EOS14950	AA532807	Hs.105822	ESTs	1.6
320793	EOS20724	AL049980	Hs.184216	DKFZP564C152 protein	1.6
305371	EOS05302	AA714180		EST singleton (not in UniGene) with exon hit	1.6
305054	EOS04985	AA634127	Hs.182426	ribosomal protein S2	1.6
314643	EOS14574	AI587502	Hs.192088	ESTs	1.6
308186	EOS08117	AI537940		EST singleton (not in UniGene) with exon hit	1.6
319371	EOS19302	R00321	Hs.174928	ESTs	1.6
331700	EOS31631	Z40011	Hs.180582	ESTs	1.6
316955	EOS16886	AW203959	Hs.149532	ESTs	1.6
314961	EOS14892	AW008061	Hs.231994	ESTs	1.6
336676	EOS36607	CH22_4154FG_43_4_		CH22_FGENES.43-4	1.6
322801	EOS22732	AI831910	Hs.163734	ESTs	1.6
303363	EOS03294	AI964095	Hs.226801	ESTs; Weakly similar to DIA-156 protein [H.sapiens]	1.6
328105	EOS28036	c_6_hs gi|5868020|ref| gn 11 - 301705 301784 ex 4 7 CDSi 5.30 80 3147		CH.06_hs gi|5868020	1.6
325481	EOS25412	c12_hs gi|5866957|ref| gn 3 + 47590 47672 ex 4 7 CDSi 2.69 83 1895		CH.12_hs gi|5866957	1.6
315361	EOS15292	AI335229	Hs.122031	ESTs	1.6
324902	EOS24833	D31323	Hs.211188	ESTs	1.6
336018	EOS35949	CH22_3401FG_669_7_LINK_DJ32I10.GENSCAN.9-12		CH22_FGENES.669_7	1.6
308747	EOS08678	AI804500	Hs.181165	eukaryotic translation elongation factor 1 alpha 1	1.6
328251	EOS28182	c_6_hs gi|6381891|ref| gn 4 + 124444 124557 ex 2 3 CDSi 0.40 114 4554		CH.06_hs gi|6381891	1.6
303153	EOS03084	U09759	Hs.8325	mitogen-activated protein kinase 9	1.6
327809	EOS27740	c_5_hs gi|5867968|ref| gn 3 + 54610 54761 ex 4 4 CDSi 0.78 152 993		CH.05_hs gi|5867968	1.6
314107	EOS14038	AA806113	Hs.189025	ESTs	1.6
300304	EOS00235	AI637934	Hs.224978	ESTs	1.6
313009	EOS12940	W52010	Hs.191379	ESTs	1.6
331074	EOS31005	R08440		yf19f9.s1 Soares fetal liver spleen 1NFLS Homo sapiens cDNA clone IMAGE:127337 3' similar to contains Alu repetitive element;, mRNA sequence	1.6
335773	EOS35704	CH22_3142FG_607_9_LINK_EM:AC005500.GENSCAN.496-4		CH22_FGENES.607_9	1.6
334991	EOS34922	CH22_2312FG_469_11_LINK_EM:AC005500.GENSCAN.365-11		CH22_FGENES.469_11	1.6
322959	EOS22890	AI267606		EST cluster (not in UniGene)	1.6

323731	EOS23662	AA323414		EST cluster (not in UniGene)	1.6
331073	EOS31004	R07998	Hs.18628	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.6
313573	EOS13504	AI076259	Hs.190337	ESTs	1.6
316949	EOS16880	AA856749	Hs.124620	ESTs	1.6
328084	EOS28015	c_6_hs gi|6469819|ref| gn 3 - 155366 155459 ex 1 4 CDSI 1.23 94 2982		CH.06_hs gi|6469819	1.6
331526	EOS31457	N49967	Hs.46624	ESTs	1.6
317987	EOS17918	AW138174	Hs.130651	ESTs	1.6
325594	EOS25525	c13_hs gi|5866992|ref| gn 4 - 470474 470566 ex 2 3 CDSI 8.09 93 68		CH.13_hs gi|5866992	1.6
310848	EOS10779	AI459554	Hs.161286	ESTs	1.6
309268	EOS09199	AI985821	Hs.62954	ferritin; heavy polypeptide 1	1.6
304518	EOS04449	AA461438		EST singleton (not in UniGene) with exon hit	1.6
331065	EOS30996	N90584	Hs.9167	Homo sapiens clone 25085 mRNA sequence	1.6
306501	EOS06432	AA987294		EST singleton (not in UniGene) with exon hit	1.6
323289	EOS23220	AL134235	Hs.222442	ESTs	1.6
334630	EOS34561	CH22_1938FG_416_6_LINK_EM:AC005500.GENSCAN.277-6		CH22_FGENES.416_6	1.6
302025	EOS01956	AI091466	Hs.127241	DKFZP564F052 protein	1.6
328998	EOS28929	c_9_hs gi|5868538|ref| gn 1 + 40996 41104 ex 1 3 CDSf 11.00 109 480		CH.09_hs gi|5868538	1.6
313197	EOS13128	AI738851	Hs.222487	ESTs	1.6
338763	EOS38694	CH22_7585FG__LINK_EM:AC005500.GENSCAN.517-16		CH22_EM:AC005500.GENSCAN.517-16	1.6
332247	EOS32178	N58172	Hs.109370	ESTs	1.6
316724	EOS16655	AA810788	Hs.123337	ESTs	1.6
303306	EOS03237	AA215297		EST cluster (not in UniGene) with exon hit	1.6
306336	EOS06267	AA954198		EST singleton (not in UniGene) with exon hit	1.6
308256	EOS08187	AI565498		EST singleton (not in UniGene) with exon hit	1.6
307056	EOS06987	AI148675		EST singleton (not in UniGene) with exon hit	1.6
321370	EOS21301	AJ227900		EST cluster (not in UniGene)	1.6
336262	EOS36193	CH22_3661FG_754_9_LINK_DA59H18.GENSCAN.57-11		CH22_FGENES.754_9	1.6
335497	EOS35428	CH22_2849FG_571_5_LINK_EM:AC005500.GENSCAN.460-26		CH22_FGENES.571_5	1.6
309582	EOS09513	AW169657		EST singleton (not in UniGene) with exon hit	1.6
329563	EOS29494	c10_p2 gi|3962490|gb|A gn 1 - 410 635 ex 2 2 CDSf 13.80 226 267		CH.10_p2 gi|3962490	1.6
332504	EOS32435	AA053917	Hs.15106	chromosome 14 open reading frame 1	1.6
308090	EOS08021	AI474601	Hs.2186	eukaryotic translation elongation factor 1 gamma	1.6
331752	EOS31683	AA287312	Hs.191648	ESTs	1.6
330881	EOS30812	AA132986	Hs.69321	ESTs; Weakly similar to Similar to mucin and several other Ser-Thr-rich proteins [S.cerevisiae]	1.6
315647	EOS15578	AA648983	Hs.212911	ESTs	1.6
336766	EOS36697	CH22_4341FG_143_20_		CH22_FGENES.143-20	1.6
302592	EOS02523	AA294921	Hs.250811	v-ral simian leukemia viral oncogene homolog B (ras related; GTP binding protein)	1.6
315076	EOS15007	AI623817	Hs.168457	ESTs	1.6
337056	EOS36987	CH22_4946FG_441_4_		CH22_FGENES.441-4	1.6
322175	EOS22106	AF085975		EST cluster (not in UniGene)	1.6
336833	EOS36764	CH22_4504FG_242_2_		CH22_FGENES.242-2	1.6
334902	EOS34833	CH22_2219FG_452_16_LINK_EM:AC005500.GENSCAN.341-19		CH22_FGENES.452_16	1.6
318671	EOS18602	AA188823	Hs.212621	ESTs	1.6
308064	EOS07995	AI469273	Hs.181165	eukaryotic translation elongation factor 1 alpha 1	1.6
320559	EOS20490	AB021981	Hs.159322	solute carrier family 35 (UDP-N-acetylglucosamine (UDP-GlcNAc) transporter); member 3	1.6
317881	EOS17812	AI827248	Hs.224398	ESTs	1.6
313078	EOS13009	N49730		EST cluster (not in UniGene)	1.6
338689	EOS38620	CH22_7464FG__LINK_EM:AC005500.GENSCAN.475-3		CH22_EM:AC005500.GENSCAN.475-3	1.6
311804	EOS11735	AA135159	Hs.203349	ESTs	1.6
316359	EOS16290	AI472213	Hs.123415	ESTs	1.6
330182	EOS30113	c_4_p2 gi|5123954|emb| gn 4 + 120156 120245 ex 2 2 CDSI 4.69 90 11		CH.04_p2 gi|5123954	1.6
334718	EOS34649	CH22_2028FG_421_29_LINK_EM:AC005500.GENSCAN.282-29		CH22_FGENES.421_29	1.6
324196	EOS24127	AA405524	Hs.178000	ESTs	1.6
305350	EOS05281	AA706676		EST singleton (not in UniGene) with exon hit	1.6
331469	EOS31400	N22273	Hs.39140	ESTs	1.6
305715	EOS05646	AA826884		EST singleton (not in UniGene) with exon hit	1.6
314460	EOS14391	AI263231	Hs.145607	ESTs	1.6
317634	EOS17565	AA953088	Hs.127550	ESTs	1.6
335293	EOS35224	CH22_2635FG_527_6_LINK_EM:AC005500.GENSCAN.421-9		CH22_FGENES.527_6	1.6
305611	EOS05542	AA782331		EST singleton (not in UniGene) with exon hit	1.6
310430	EOS10361	AI670843	Hs.200257	ESTs	1.6
323696	EOS23627	AA641201	Hs.222051	ESTs	1.6
300610	EOS00541	N72596	Hs.99120	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide; Y chromosome	1.6
327364	EOS27295	c_1_hs gi|6552412|ref| gn 2 - 115235 115396 ex 1 9 CDSI 2.77 162 3007		CH.01_hs gi|6552412	1.6
324848	EOS24779	AW021857		EST cluster (not in UniGene)	1.6
321491	EOS21422	H70665	Hs.183960	ESTs	1.6
336367	EOS36298	CH22_3779FG_818_11_LINK_BA232E17.GENSCAN.3-17		CH22_FGENES.818_11	1.6
331549	EOS31480	N56866	Hs.237507	EST	1.6
328332	EOS28263	c_7_hs gi|5868375|ref| gn 6 + 280154 280289 ex 3 5 CDSI -1.04 136 516		CH.07_hs gi|5868375	1.5
322817	EOS22748	C02420		EST cluster (not in UniGene)	1.5

303983	EOS03914	AW514111	Hs.181165	eukaryotic translation elongation factor 1 alpha 1	1.5
329434	EOS29365	c_y_hs gi|5868883|ref| gn 1 - 31124 31263 ex 3 20 CDSI 6.38 140 241		CH.Y_hs gi|5868883	1.5
338196	EOS38127	CH22_6763FG__LINK_EM:AC005500.GENSCAN.235-16		CH22_EM:AC005500.GENSCAN.235-16	1.5
308488	EOS08419	AI682148	Hs.179661	Homo sapiens clone 24703 beta-tubulin mRNA; complete cds	1.5
314883	EOS14814	AW178807	Hs.246182	ESTs	1.5
307095	EOS07026	AI167910		EST singleton (not in UniGene) with exon hit	1.5
306953	EOS06884	AI124971		EST singleton (not in UniGene) with exon hit	1.5
331786	EOS31717	AA398539	Hs.97369	EST	1.5
303509	EOS03440	AW378236	Hs.256050	ESTs	1.5
324515	EOS24446	AW501686	Hs.163539	ESTs	1.5
339323	EOS39254	CH22_8284FG__LINK_BA354I12.GENSCAN.23-2		CH22_BA354I12.GENSCAN.23-2	1.5
306563	EOS06494	AA995296		EST singleton (not in UniGene) with exon hit	1.5
316076	EOS16007	AW297895	Hs.116424	ESTs	1.5
325622	EOS25553	c14_hs gi|5867000|ref| gn 2 + 69994 70075 ex 6 8 CDSI 9.40 82 194		CH.14_hs gi|5867000	1.5
309632	EOS09563	AW193261	Hs.156110	Immunoglobulin kappa variable 1D-8	1.5
314926	EOS14857	AI380838	Hs.124835	ESTs	1.5
314458	EOS14389	AI217440	Hs.143873	ESTs	1.5
335219	EOS35150	CH22_2558FG_513_2_LINK_EM:AC005500.GENSCAN.406-2		CH22_FGENES.513_2	1.5
301079	EOS01010	AA305047	Hs.183654	ESTs; Weakly similar to unknown [S.cerevisiae]	1.5
334122	EOS34053	CH22_1400FG_333_3_LINK_EM:AC005500.GENSCAN.185-27		CH22_FGENES.333_3	1.5
308139	EOS08070	AI494477		EST singleton (not in UniGene) with exon hit	1.5
317412	EOS17343	AI301528	Hs.132604	ESTs	1.5
315073	EOS15004	AW452948	Hs.257631	ESTs	1.5
313139	EOS13070	AA362113		EST cluster (not in UniGene)	1.5
307012	EOS06943	AI140212		EST singleton (not in UniGene) with exon hit	1.5
322895	EOS22826	AW470295	Hs.192152	ESTs	1.5
303779	EOS03710	AA897296	Hs.221266	ESTs	1.5
312344	EOS12275	AI742618	Hs.181733	ESTs; Weakly similar to nitrilase homolog 1 [H.sapiens]	1.5
323632	EOS23563	AL039950		EST cluster (not in UniGene)	1.5
332336	EOS32267	T96130	Hs.137551	ESTs	1.5
304547	EOS04478	AA486189		EST singleton (not in UniGene) with exon hit	1.5
335692	EOS35623	CH22_3053FG_596_7_LINK_EM:AC005500.GENSCAN.488-7		CH22_FGENES.596_7	1.5
328333	EOS28264	c_7_hs gi|5868375|ref| gn 6 + 282506 282664 ex 4 5 CDSI 7.71 159 517		CH.07_hs gi|5868375	1.5
304143	EOS04074	R88737		EST singleton (not in UniGene) with exon hit	1.5
329625	EOS29556	c11_p2 gi|4567169|gb|A gn 2 - 85893 85984 ex 3 5 CDSI 2.24 92 29		CH.11_p2 gi|4567169	1.5
329960	EOS29891	c16_p2 gi|5091594|gb|A gn 1 - 1031 1162 ex 1 3 CDSI 10.75 132 415		CH.16_p2 gi|5091594	1.5
318975	EOS18906	Z44110		EST cluster (not in UniGene)	1.5
321875	EOS21806	N49122		EST cluster (not in UniGene)	1.5
320451	EOS20382	R26944	Hs.180777	Homo sapiens mRNA; cDNA DKFZp564M0264 (from clone DKFZp564M0264)	1.5
336020	EOS35951	CH22_3403FG_669_9_LINK_DJ32I10.GENSCAN.9-14		CH22_FGENES.669_9	1.5
332581	EOS32512	T28799	Hs.2913	EphB3	1.5
338622	EOS38553	CH22_7384FG__LINK_EM:AC005500.GENSCAN.451-1		CH22_EM:AC005500.GENSCAN.451-1	1.5
330397	EOS30328	D14659	Hs.154387	KIAA0103 gene product	1.5
314359	EOS14290	AA205569	Hs.194193	ESTs	1.5
313456	EOS13387	AW380579	Hs.209657	ESTs	1.5
318486	EOS18417	H09123	Hs.139258	ESTs	1.5
318175	EOS18106	AA644624		EST cluster (not in UniGene)	1.5
335684	EOS35615	CH22_3045FG_595_4_LINK_EM:AC005500.GENSCAN.487-13		CH22_FGENES.595_4	1.5
327814	EOS27745	c_5_hs gi|5867968|ref| gn 6 + 69377 70566 ex 1 2 CDSf 86.15 1190 999		CH.05_hs gi|5867968	1.5
322120	EOS22051	W84351	Hs.213846	ESTs	1.5
311749	EOS11680	R06249	Hs.13911	ESTs	1.5
329797	EOS29728	c14_p2 gi|6523160|emb| gn 1 - 10616 10894 ex 3 6 CDSI 5.86 279 1549		CH.14_p2 gi|6523160	1.5
330630	EOS30561	X78669	Hs.79088	reticulocalbin 2; EF-hand calcium binding domain	1.5
303777	EOS03708	AA348491		EST cluster (not in UniGene) with exon hit	1.5
309656	EOS09587	AW197060	Hs.195188	glyceraldehyde-3-phosphate dehydrogenase	1.5
326165	EOS26096	c17_hs gi|5867208|ref| gn 2 - 62787 62929 ex 1 10 CDSI 0.87 143 2037		CH.17_hs gi|5867208	1.5
308328	EOS08259	AI590571	Hs.186412	EST	1.5
300601	EOS00532	AI762130	Hs.165619	ESTs	1.5
303610	EOS03541	AA323288		EST cluster (not in UniGene) with exon hit	1.5
307856	EOS07787	AI366158		EST singleton (not in UniGene) with exon hit	1.5
319920	EOS19851	R54575	Hs.13337	ESTs; Weakly similar to similar to Phosphoglucomutase and phosphomannomutase phosphoserine [C.elegans]	1.5
332167	EOS32098	D57389	Hs.75447	ralA binding protein 1	1.5
316427	EOS16358	AI241019	Hs.145644	ESTs	1.5
303886	EOS03817	AW365963		EST cluster (not in UniGene) with exon hit	1.5
314292	EOS14223	AA732590	Hs.134740	ESTs	1.5
315408	EOS15339	AW273261	Hs.216292	ESTs	1.5
335698	EOS35629	CH22_3059FG_597_1_LINK_EM:AC005500.GENSCAN.489-1		CH22_FGENES.597_1	1.5
315084	EOS15015	AI821085	Hs.187796	ESTs	1.5

302299	EOS02230	R64632	Hs.182167	hemoglobin; gamma A	1.5
306803	EOS06734	AI055860	Hs.193717	interleukin 10	1.5
315802	EOS15733	AA677540	Hs.117064	ESTs	1.5
326257	EOS26188	c17_hs gi|5867264|ref| gn 6 + 222712 222819 ex 2 2 CDSI 4.46 108 3597		CH.17_hs gi|5867264	1.5
319599	EOS19530	H56112		EST cluster (not in UniGene)	1.5
321891	EOS21822	AW157424	Hs.165954	ESTs	1.5
335164	EOS35095	CH22_2500FG_502_8_LINK_EM:AC005500.GENSCAN.396-23		CH22_FGENES.502_8	1.5
327133	EOS27064	c21_hs gi|6682522|ref| gn 1 + 38069 38938 ex 2 2 CDSI 63.42 870 1583		CH.21_hs gi|6682522	1.5
317460	EOS17391	AA926980	Hs.131347	ESTs	1.5
332344	EOS32275	W45574	Hs.252497	ESTs	1.5
328801	EOS28732	c_7_hs gi|5868321|ref| gn 1 - 44492 44609 ex 2 3 CDSI 1.71 118 5525		CH.07_hs gi|5868321	1.5
321677	EOS21608	N44545	Hs.251865	ESTs	1.5
331858	EOS31789	AA421163	Hs.163848	ESTs	1.5
309243	EOS09174	AI972052		EST singleton (not in UniGene) with exon hit	1.5
326213	EOS26144	c17_hs gi|5867224|ref| gn 3 - 60751 60927 ex 1 4 CDSI 2.06 177 2687		CH.17_hs gi|5867224	1.5
321632	EOS21563	AA419617		EST cluster (not in UniGene)	1.5
321424	EOS21355	AA057301		EST cluster (not in UniGene)	1.5
322465	EOS22396	AA137152	Hs.3784	ESTs; *Highly similar to phosphoserine aminotransferase [H.sapiens]*	1.5
333391	EOS33322	CH22_637FG_144_6_LINK_EM:AC005500.GENSCAN.25-6		CH22_FGENES.144_6	1.5
333384	EOS33315	CH22_630FG_143_23_LINK_EM:AC005500.GENSCAN.24-17		CH22_FGENES.143_23	1.5
334784	EOS34715	CH22_2096FG_432_9_LINK_EM:AC005500.GENSCAN.293-12		CH22_FGENES.432_9	1.5
334078	EOS34009	CH22_1356FG_327_33_LINK_EM:AC005500.GENSCAN.181-35		CH22_FGENES.327_33	1.5
335158	EOS35089	CH22_2494FG_502_2_LINK_EM:AC005500.GENSCAN.396-17		CH22_FGENES.502_2	1.5
335062	EOS34993	CH22_2388FG_482_17_LINK_EM:AC005500.GENSCAN.376-16		CH22_FGENES.482_17	1.5
333243	EOS33174	CH22_482FG_111_7_LINK_EM:AC000097.GENSCAN.120-6		CH22_FGENES.111_7	1.5
306380	EOS06311	AA968861		EST singleton (not in UniGene) with exon hit	1.5
320809	EOS20740	AI540299		EST cluster (not in UniGene)	1.5
332813	EOS32744	CH22_29FG_8_1_LINK_C65E1.GENSCAN.2-2		CH22_FGENES.8_1	1.5
335817	EOS35748	CH22_3189FG_618_5_LINK_EM:AC005500.GENSCAN.510-5		CH22_FGENES.618_5	1.5
319551	EOS19482	AA761668		EST cluster (not in UniGene)	1.5
334472	EOS34403	CH22_1771FG_394_3_LINK_EM:AC005500.GENSCAN.257-3		CH22_FGENES.394_3	1.5
333029	EOS32960	CH22_255FG_68_3_LINK_EM:AC000097.GENSCAN.40-3		CH22_FGENES.68_3	1.5
308055	EOS07986	AI468091	Hs.119252	tumor protein; translationally-controlled 1	1.5
302882	EOS02813	AW403330		EST cluster (not in UniGene) with exon hit	1.5
314033	EOS13964	AA167125		EST cluster (not in UniGene)	1.5
324928	EOS24859	AI932285	Hs.160569	ESTs	1.5
329524	EOS29455	c10_p2 gi|3983507|gb|A gn 6 - 38025 38143 ex 3 3 CDSI 2.40 119 170		CH.10_p2 gi|3983507	1.5
333131	EOS33062	CH22_360FG_83_6_LINK_EM:AC000097.GENSCAN.67-10		CH22_FGENES.83_6	1.5
332085	EOS32016	AA600353	Hs.173933	ESTs; Weakly similar to NUCLEAR FACTOR 1/X [H.sapiens]	1.5
305369	EOS05300	AA714040		EST singleton (not in UniGene) with exon hit	1.5
300344	EOS00275	AW291487	Hs.213659	ESTs	1.5
325071	EOS25002	H09693		EST cluster (not in UniGene)	1.5
323693	EOS23624	AW297758	Hs.249721	ESTs	1.5
321899	EOS21830	N55158	Hs.135252	ESTs	1.5
331857	EOS31788	AA421160	Hs.9456	SWI/SNF related; matrix associated; actin dependent regulator of chromatin; subfamily a; member 5	1.5
334850	EOS34781	CH22_2164FG_439_36_LINK_EM:AC005500.GENSCAN.311-13		CH22_FGENES.439_36	1.5
322610	EOS22541	AF180919		EST cluster (not in UniGene)	1.5
335332	EOS35263	CH22_2677FG_535_6_LINK_EM:AC005500.GENSCAN.426-6		CH22_FGENES.535_6	1.5
307565	EOS07496	AI282468		EST singleton (not in UniGene) with exon hit	1.5
314140	EOS14071	AI216473	Hs.154297	ESTs	1.5
323011	EOS22942	AA580288		EST cluster (not in UniGene)	1.5
325366	EOS25297	c12_hs gi|5866920|ref| gn 9 - 920962 921713 ex 1 8 CDSI 15.95 752 167		CH.12_hs gi|5866920	1.5
322306	EOS22237	W75935	Hs.146083	ESTs	1.5
311034	EOS10965	AI564023	Hs.171467	ESTs; Highly similar to NKG2-D TYPE II INTEGRAL MEMBRANE PROTEIN [H.sapiens]	1.5
305081	EOS05012	AA641638		EST singleton (not in UniGene) with exon hit	1.5
322933	EOS22864	AA099759		EST cluster (not in UniGene)	1.5
335221	EOS35152	CH22_2560FG_513_4_LINK_EM:AC005500.GENSCAN.406-4		CH22_FGENES.513_4	1.5
304948	EOS04879	AA613107		EST singleton (not in UniGene) with exon hit	1.5
334900	EOS34831	CH22_2217FG_452_14_LINK_EM:AC005500.GENSCAN.341-17		CH22_FGENES.452_14	1.5
318404	EOS18335	AI654108	Hs.135125	ESTs	1.5
339358	EOS39289	CH22_8328FG__LINK_BA354I12.GENSCAN.31-3		CH22_BA354I12.GENSCAN.31-3	1.5
327074	EOS27005	c21_hs gi|6531965|ref| gn 58 + 4039993 4040096 ex 3 4 CDSI 0.68 104 1284			

				CH.21_hs gi|6531965	1.5
326054	EOS25985	c17_hs gi|5867184|ref| gn 2 - 146342 146469 ex 3 4 CDSI 10.00 128 426		CH.17_hs gi|5867184	1.5
326892	EOS26823	c20_hs gi|6682511|ref| gn 5 + 119424 119500 ex 29 30 CDSI 18.89 77 2313		CH.20_hs gi|6682511	1.5
328767	EOS28698	c_7_hs gi|6017031|ref| gn 1 - 35625 35723 ex 4 4 CDSI 5.63 99 5262		CH.07_hs gi|6017031	1.5
337772	EOS37703	CH22_6125FG__LINK_EM:AC000097.GENSCAN.119-11		CH22_EM:AC000097.GENSCAN.119-11	1.5
312199	EOS12130	AW438602	Hs.191179	ESTs	1.5
303506	EOS03437	AA340605	Hs.105887	ESTs	1.5
325176	EOS25107	T52843		EST cluster (not in UniGene)	1.5
302023	EOS01954	AF060567	Hs.126782	sushi-repeat protein	1.5
305833	EOS05764	AA857836	Hs.181165	eukaryotic translation elongation factor 1 alpha 1	1.5
309131	EOS09062	AI929175	Hs.119122	ribosomal protein L13a	1.5
334184	EOS34115	CH22_1465FG_350_15_LINK_EM:AC005500.GENSCAN.209-17		CH22_FGENES.350_15	1.5
335188	EOS35119	CH22_2524FG_507_3_LINK_EM:AC005500.GENSCAN.400-3		CH22_FGENES.507_3	1.5
304813	EOS04744	AA584540		EST singleton (not in UniGene) with exon hit	1.5
315359	EOS15290	AA608808	Hs.225118	ESTs	1.5
324434	EOS24365	AA707249	Hs.98789	ESTs	1.5
327910	EOS27841	c_6_hs gi|5868162|ref| gn 1 + 21622 21748 ex 6 7 CDSI 3.69 127 449		CH.06_hs gi|5868162	1.4
335671	EOS35602	CH22_3031FG_592_3_LINK_EM:AC005500.GENSCAN.485-4		CH22_FGENES.592_3	1.4
334943	EOS34874	CH22_2264FG_465_8_LINK_EM:AC005500.GENSCAN.359-8		CH22_FGENES.465_8	1.4
326393	EOS26324	c19_hs gi|5867341|ref| gn 2 + 41702 41841 ex 5 5 CDSI 20.15 140 504		CH.19_hs gi|5867341	1.4
305296	EOS05227	AA687181		EST singleton (not in UniGene) with exon hit	1.4
307243	EOS07174	AI199957		EST singleton (not in UniGene) with exon hit	1.4
320066	EOS19997	AW364885	Hs.112442	ESTs	1.4
311465	EOS11396	AI758660	Hs.206132	ESTs	1.4
302822	EOS02753	AW404176	Hs.111611	ribosomal protein L27	1.4
304987	EOS04918	AA618044		EST singleton (not in UniGene) with exon hit	1.4
330892	EOS30823	AA149579	Hs.118258	ESTs	1.4
333385	EOS33316	CH22_631FG_143_24_LINK_EM:AC005500.GENSCAN.24-18		CH22_FGENES.143_24	1.4
302626	EOS02557	AB021870		EST cluster (not in UniGene) with exon hit	1.4
318042	EOS17973	AW294522	Hs.149991	ESTs	1.4
339361	EOS39292	CH22_8331FG__LINK_BA354I12.GENSCAN.32-3		CH22_BA354I12.GENSCAN.32-3	1.4
309000	EOS08931	AI880489		EST singleton (not in UniGene) with exon hit	1.4
306004	EOS05935	AA889992		EST singleton (not in UniGene) with exon hit	1.4
329539	EOS29470	c10_p2 gi|3983503|gb|U gn 1 - 1 326 ex 1 3 CDSI 41.66 326 212		CH.10_p2 gi|3983503	1.4
313663	EOS13594	AI953261	Hs.169813	ESTs	1.4
323538	EOS23469	AW247696		EST cluster (not in UniGene)	1.4
337595	EOS37526	CH22_5884FG__LINK_C20H12.GENSCAN.8-1		CH22_C20H12.GENSCAN.8-1	1.4
303149	EOS03080	AA312995		EST cluster (not in UniGene) with exon hit	1.4
308484	EOS08415	AI679292		EST singleton (not in UniGene) with exon hit	1.4
300912	EOS00843	AW138724	Hs.168974	ESTs	1.4
315158	EOS15089	AA744438	Hs.142476	ESTs; Weakly similar to !!!! ALU CLASS D WARNING ENTRY !!!! [H.sapiens]	1.4
300462	EOS00393	AA746501	Hs.14217	ESTs	1.4
312730	EOS12661	AI804372	Hs.208661	ESTs	1.4
316868	EOS16799	AI660898	Hs.195602	ESTs	1.4
337629	EOS37560	CH22_5933FG__LINK_C20H12.GENSCAN.28-35		CH22_C20H12.GENSCAN.28-35	1.4
332518	EOS32449	D16562	Hs.155433	ATP synthase; H+ transporting; mitochondrial F1 complex; gamma polypeptide 1	1.4
337422	EOS37353	CH22_5624FG_760_2_		CH22_FGENES.760-2	1.4
328835	EOS28766	c_7_hs gi|5868339|ref| gn 5 + 88053 88461 ex 3 3 CDSI 13.78 409 5775		CH.07_hs gi|5868339	1.4
338282	EOS38213	CH22_6897FG__LINK_EM:AC005500.GENSCAN.291-4		CH22_EM:AC005500.GENSCAN.291-4	1.4
337895	EOS37826	CH22_6303FG__LINK_EM:AC005500.GENSCAN.56-2		CH22_EM:AC005500.GENSCAN.56-2	1.4
320330	EOS20261	AF026004	Hs.141660	chloride channel 2	1.4
314302	EOS14233	AA813118	Hs.163230	ESTs	1.4
313280	EOS13211	AI285537	Hs.222830	ESTs	1.4
333222	EOS33153	CH22_459FG_105_2_LINK_EM:AC000097.GENSCAN.109-6		CH22_FGENES.105_2	1.4
305726	EOS05657	AA828156		EST singleton (not in UniGene) with exon hit	1.4
312674	EOS12605	AI762475	Hs.151327	ESTs; Moderately similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.4
315869	EOS15800	AI033547	Hs.132826	ESTs	1.4
327010	EOS26941	c21_hs gi|5867664|ref| gn 12 + 941057 941139 ex 9 9 CDSI 7.44 83 790		CH.21_hs gi|5867664	1.4
325892	EOS25823	c16_hs gi|5867088|ref| gn 1 - 10498 10652 ex 2 3 CDSI 3.94 155 870		CH.16_hs gi|5867088	1.4
302575	EOS02506	AF071164	Hs.249171	homeo box A11	1.4
301970	EOS01901	AB028962	Hs.120245	KIAA1039 protein	1.4
332207	EOS32138	H61475	Hs.237353	EST	1.4
316024	EOS15955	AA707141	Hs.193388	ESTs	1.4
314599	EOS14530	AW206512	Hs.186996	ESTs	1.4
333585	EOS33516	CH22_846FG_203_4_LINK_EM:AC005500.GENSCAN.74-6			

				CH22_FGENES.203_4	1.4
324670	EOS24601	AI525557		EST cluster (not in UniGene)	1.4
321307	EOS21238	R85409		EST cluster (not in UniGene)	1.4
335170	EOS35101	CH22_2506FG_503_1_LINK_EM:AC005500.GENSCAN.397-1			
				CH22_FGENES.503_1	1.4
328274	EOS28205	c_7_hs gi|5868219|ref| gn 2 - 31244 31439 ex 1 11 CDSI 13.06 196 9			
				CH.07_hs gi|5868219	1.4
336880	EOS36811	CH22_4619FG_318_8_		CH22_FGENES.318-8	1.4
313825	EOS13756	AA215470		EST cluster (not in UniGene)	1.4
318410	EOS18341	AI138418	Hs.144935	ESTs	1.4
335361	EOS35292	CH22_2710FG_541_11_LINK_EM:AC005500.GENSCAN.431-16			
				CH22_FGENES.541_11	1.4
319802	EOS19733	AI701489	Hs.202501	ESTs	1.4
334769	EOS34700	CH22_2081FG_429_4_LINK_EM:AC005500.GENSCAN.290-9			
				CH22_FGENES.429_4	1.4
312709	EOS12640	AW069181	Hs.141146	ESTs; Weakly similar to transformation-related protein [H.sapiens]	1.4
330004	EOS29935	c16_p2 gi|6623963|gb|A gn 5 - 78872 78999 ex 2 6 CDSI 19.93 128 728			
				CH.16_p2 gi|6623963	1.4
313103	EOS13034	AI184303	Hs.143806	ESTs	1.4
326359	EOS26290	c18_hs gi|5867293|ref| gn 1 + 9436 9494 ex 2 3 CDSI 2.16 59 88			
				CH.18_hs gi|5867293	1.4
305211	EOS05142	AA668563		EST singleton (not in UniGene) with exon hit	1.4
334628	EOS34559	CH22_1936FG_416_4_LINK_EM:AC005500.GENSCAN.277-4			
				CH22_FGENES.416_4	1.4
326919	EOS26850	c21_hs gi|6456782|ref| gn 2 - 40486 41046 ex 1 5 CDSI 17.70 561 157			
				CH.21_hs gi|6456782	1.4
315527	EOS15458	AI791138	Hs.116768	ESTs	1.4
306090	EOS06021	AA908609		EST singleton (not in UniGene) with exon hit	1.4
303316	EOS03247	AF033122	Hs.14125	p53 regulated PA26 nuclear protein	1.4
303642	EOS03573	AW299459		EST cluster (not in UniGene) with exon hit	1.4
314357	EOS14288	AA781795	Hs.122587	ESTs	1.4
337102	EOS37033	CH22_5033FG_472_7_		CH22_FGENES.472-7	1.4
304384	EOS04315	AA235482	Hs.62954	ferritin; heavy polypeptide 1	1.4
315117	EOS15048	AA828609	Hs.192044	ESTs	1.4
305750	EOS05681	AA835250		EST singleton (not in UniGene) with exon hit	1.4
311726	EOS11657	AW081766	Hs.253920	ESTs	1.4
326996	EOS26927	c21_hs gi|5867660|ref| gn 4 - 63212 63404 ex 2 6 CDSi 15.70 193 622			
				CH.21_hs gi|5867660	1.4
330257	EOS30188	c_5_p2 gi|6671881|gb|A gn 2 - 143228 143393 ex 1 9 CDSI 11.31 166 586			
				CH.05_p2 gi|6671881	1.4
323864	EOS23795	AA340724	Hs.214028	ESTs	1.4
338204	EOS38135	CH22_6773FG__LINK_EM:AC005500.GENSCAN.241-3			
				CH22_EM:AC005500.GENSCAN.241-3	1.4
314025	EOS13956	AI983981	Hs.189114	ESTs	1.4
315974	EOS15905	AW029203	Hs.191952	ESTs	1.4
335599	EOS35530	CH22_2957FG_581_39_LINK_EM:AC005500.GENSCAN.476-37			
				CH22_FGENES.581_39	1.4
335364	EOS35295	CH22_2713FG_543_2_LINK_EM:AC005500.GENSCAN.432-4			
				CH22_FGENES.543_2	1.4
303634	EOS03565	AI953377	Hs.169425	ESTs; Weakly similar to predicted using Genefinder [C.elegans]	1.4
315626	EOS15557	AA808598	Hs.35353	ESTs; Weakly similar to H21P03.2 [C.elegans]	1.4
329936	EOS29867	c16_p2 gi|6165200|gb|A gn 4 - 82761 82920 ex 3 4 CDSi 1.15 160 199			
				CH.16_p2 gi|6165200	1.4
328632	EOS28563	c_7_hs gi|5868247|ref| gn 1 + 76734 76853 ex 1 4 CDSf 13.95 120 3764			
				CH.07_hs gi|5868247	1.4
330207	EOS30138	c_5_p2 gi|6013606|gb|A gn 3 - 109912 110004 ex 2 4 CDSI 6.54 93 174			
				CH.05_p2 gi|6013606	1.4
329919	EOS29850	c16_p2 gi|6223624|gb|A gn 6 - 103492 103681 ex 1 8 CDSI 6.18 190 93			
				CH.16_p2 gi|6223624	1.4
331916	EOS31847	AA446131	Hs.124918	ESTs	1.4
317617	EOS17548	T58194		EST cluster (not in UniGene)	1.4
331943	EOS31874	AA453418	Hs.178272	ESTs	1.4
306413	EOS06344	AA973288		EST singleton (not in UniGene) with exon hit	1.4
313607	EOS13538	N94169	Hs.194258	ESTs; Moderately similar to !!!! ALU SUBFAMILY SC WARNING ENTRY !!!! [H.sapiens]	1.4
336292	EOS36223	CH22_3691FG_783_3_LINK_BA354I12.GENSCAN.4-7			
				CH22_FGENES.783_3	1.4
330453	EOS30384	HG3976-HT4246		Pou-Domain Dna Binding Factor Pit1, Pituitary-Specific	1.4
324602	EOS24533	AA503620	Hs.213239	ESTs	1.4
332183	EOS32114	H08225	Hs.177181	ESTs	1.4
320032	EOS19963	AI699772	Hs.202361	ESTs; Weakly similar to X-linked retinopathy protein [H.sapiens]	1.4
333156	EOS33087	CH22_387FG_89_6_LINK_EM:AC000097.GENSCAN.84-8			
				CH22_FGENES.89_6	1.4
334156	EOS34087	CH22_1435FG_340_6_LINK_EM:AC005500.GENSCAN.190-7			
				CH22_FGENES.340_6	1.4
334303	EOS34234	CH22_1594FG_373_6_LINK_EM:AC005500.GENSCAN.233-5			
				CH22_FGENES.373_6	1.4
325513	EOS25444	c12_hs gi|6017035|ref| gn 1 - 34295 34490 ex 2 7 CDSi 6.49 196 2471			
				CH.12_hs gi|6017035	1.4
302758	EOS02689	AA984563		EST cluster (not in UniGene) with exon hit	1.4
329557	EOS29488	c10_p2 gi|3962492|gb|A gn 6 - 53197 53647 ex 2 2 CDSf 37.68 451 247			
				CH.10_p2 gi|3962492	1.4
331717	EOS31648	AA190888	Hs.153881	ESTs; Highly similar to NY-REN-62 antigen [H.sapiens]	1.4
325885	EOS25816	c16_hs gi|5867087|ref| gn 11 + 193212 193377 ex 1 3 CDSf 43.19 166 792			
				CH.16_hs gi|5867087	1.4
312160	EOS12091	AA805903	Hs.184371	ESTs	1.4
328882	EOS28813	c_7_hs gi|6552423|ref| gn 2 - 157669 157826 ex 4 6 CDSi 4.91 158 6200			

				CH.07_hs gi|6552423	1.4
339028	EOS38959	CH22_7925FG__LINK_DA59H18.GENSCAN.22-8		CH22_DA59H18.GENSCAN.22-8	1.4
323497	EOS23428	AI523613	Hs.221544	ESTs	1.4
316897	EOS16828	AA838114		EST cluster (not in UniGene)	1.4
312479	EOS12410	AI950844	Hs.128738	ESTs; Weakly similar to non-lens beta gamma-crystallin like protein [H.sapiens]	1.4
338535	EOS38466	CH22_7251FG__LINK_EM:AC005500.GENSCAN.404-3		CH22_EM:AC005500.GENSCAN.404-3	1.4
312754	EOS12685	R99834	Hs.250383	ESTs	1.4
327527	EOS27458	c_2_hs gi|6381882|ref| gn 2 - 98950 99040 ex 4 8 CDSi 5.78 91 1768		CH.02_hs gi|6381882	1.4
324714	EOS24645	AA574312	Hs.245737	ESTs	1.4
302347	EOS02278	AF039400	Hs.194659	chloride channel; calcium activated; family member 1	1.4
338008	EOS37939	CH22_6490FG__LINK_EM:AC005500.GENSCAN.127-9		CH22_EM:AC005500.GENSCAN.127-9	1.4
315590	EOS15521	AA640637	Hs.225817	ESTs	1.4
320825	EOS20756	NM_004751		EST cluster (not in UniGene)	1.4
300930	EOS00861	AI289481	Hs.136371	ESTs	1.4
335225	EOS35156	CH22_2564FG_513_10_LINK_EM:AC005500.GENSCAN.406-9		CH22_FGENES.513_10	1.4
337303	EOS37234	CH22_5442FG_681_5_		CH22_FGENES.681-5	1.4
317198	EOS17129	AI810384	Hs.128025	ESTs	1.4
308991	EOS08922	AI879831		EST singleton (not in UniGene) with exon hit	1.4
325472	EOS25403	c12_hs gi|6017034|ref| gn 7 - 289581 289657 ex 2 6 CDSi 4.74 77 1786		CH.12_hs gi|6017034	1.4
301266	EOS01197	AA829774		EST cluster (not in UniGene) with exon hit	1.4
330901	EOS30832	AA157818	Hs.238380	Human endogenous retroviral protease mRNA; complete cds	1.4
313406	EOS13337	AI248314	Hs.132932	ESTs	1.4
301454	EOS01385	AI751738		EST cluster (not in UniGene) with exon hit	1.4
317269	EOS17200	AA906411	Hs.127378	ESTs	1.4
338876	EOS38807	CH22_7733FG__LINK_DJ32I10.GENSCAN.4-2		CH22_DJ32I10.GENSCAN.4-2	1.4
328481	EOS28412	c_7_hs gi|5868449|ref| gn 1 - 8987 9180 ex 4 31 CDSi 10.00 194 2103		CH.07_hs gi|5868449	1.4
314022	EOS13953	AW452420	Hs.248678	ESTs	1.4
307640	EOS07571	AI301992		EST singleton (not in UniGene) with exon hit	1.4
315541	EOS15472	AI168233	Hs.123159	ESTs; Weakly similar to KIAA0668 protein [H.sapiens]	1.4
315489	EOS15420	AA628245	Hs.191847	ESTs	1.4
327815	EOS27746	c_5_hs gi|5867968|ref| gn 6 + 70804 71401 ex 2 2 CDSI 27.99 598 1000		CH.05_hs gi|5867968	1.4
339319	EOS39250	CH22_8280FG__LINK_BA354I12.GENSCAN.22-19		CH22_BA354I12.GENSCAN.22-19	1.4
322564	EOS22495	W86440	Hs.118344	ESTs	1.4
323812	EOS23743	AW081373	Hs.199199	ESTs	1.4
303540	EOS03471	AA355607	Hs.173590	ESTs; Weakly similar to MMSET type I [H.sapiens]	1.4
337902	EOS37833	CH22_6314FG__LINK_EM:AC005500.GENSCAN.56-13		CH22_EM:AC005500.GENSCAN.56-13	1.4
335289	EOS35220	CH22_2631FG_527_2_LINK_EM:AC005500.GENSCAN.421-2		CH22_FGENES.527_2	1.4
327919	EOS27850	c_6_hs gi|5868165|ref| gn 6 + 547701 547800 ex 14 14 CDSI -0.20 100 505		CH.06_hs gi|5868165	1.4
337674	EOS37605	CH22_6005FG__LINK_EM:AC000097.GENSCAN.67-4		CH22_EM:AC000097.GENSCAN.67-4	1.4
320087	EOS20018	AF032387	Hs.113265	small nuclear RNA activating complex; polypeptide 4; 190kD	1.4
334939	EOS34870	CH22_2259FG_465_3_LINK_EM:AC005500.GENSCAN.359-3		CH22_FGENES.465_3	1.3
303443	EOS03374	AA320525		EST cluster (not in UniGene) with exon hit	1.3
325929	EOS25860	c16_hs gi|5867125|ref| gn 2 - 51715 51996 ex 1 1 CDSo 29.05 282 1594		CH.16_hs gi|5867125	1.3
327745	EOS27676	c_5_hs gi|6531959|ref| gn 1 - 229066 229124 ex 3 6 CDSI 3.01 59 177		CH.05_hs gi|6531959	1.3
335166	EOS35097	CH22_2502FG_502_10_LINK_EM:AC005500.GENSCAN.396-25		CH22_FGENES.502_10	1.3
324497	EOS24428	AW152624	Hs.136340	ESTs	1.3
338374	EOS38305	CH22_7017FG__LINK_EM:AC005500.GENSCAN.327-1		CH22_EM:AC005500.GENSCAN.327-1	1.3
313601	EOS13532	R32458	Hs.257711	ESTs	1.3
321415	EOS21346	AI377596	Hs.3337	transmembrane 4 superfamily member 1	1.3
305309	EOS05240	AA699717		EST singleton (not in UniGene) with exon hit	1.3
330447	EOS30378	HG3546-HT3744		Pre-Mrna Splicing Factor Sf2p33, Alt. Splice Form 1	1.3
308578	EOS08509	AI708573		EST singleton (not in UniGene) with exon hit	1.3
315344	EOS15275	AW292176	Hs.245834	ESTs	1.3
330503	EOS30434	M55024		Human cell surface glycoprotein P3.58 mRNA, partial cds	1.3
308227	EOS08158	AI559126	Hs.195188	glyceraldehyde-3-phosphate dehydrogenase	1.3
332222	EOS32153	N28271	Hs.176618	ESTs	1.3
323961	EOS23892	AL044428	Hs.207345	ESTs	1.3
314530	EOS14461	AI052358	Hs.131741	ESTs	1.3
320503	EOS20434	NM_005897		EST cluster (not in UniGene)	1.3
306820	EOS06751	AI074408		EST singleton (not in UniGene) with exon hit	1.3
304165	EOS04096	H73265		EST singleton (not in UniGene) with exon hit	1.3
324302	EOS24233	AA543008	Hs.136806	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.3
319128	EOS19059	AA393820		EST cluster (not in UniGene)	1.3
317092	EOS17023	AI286162	Hs.125657	ESTs	1.3
304998	EOS04929	AA621203		EST singleton (not in UniGene) with exon hit	1.3
331433	EOS31364	H68097	Hs.161023	EST	1.3
333348	EOS33279	CH22_594FG_140_2_LINK_EM:AC005500.GENSCAN.20-2			

				CH22_FGENES.140_2	1.3
333619	EOS33550	CH22_880FG_219_3_LINK_EM:AC005500.GENSCAN.87-2		CH22_FGENES.219_3	1.3
335903	EOS35834	CH22_3280FG_635_11_LINK_EM:AC005500.GENSCAN.525-14		CH22_FGENES.635_11	1.3
326219	EOS26150	c17_hs gi|5867226|ref| gn 11 - 264008 264274 ex 3 5 CDSI 5.74 267 2847		CH.17_hs gi|5867226	1.3
324456	EOS24387	AW500954		EST cluster (not in UniGene)	1.3
316405	EOS16336	AA757900	Hs.202624	ESTs	1.3
314361	EOS14292	AL038765	Hs.161304	ESTs	1.3
328546	EOS28477	c_7_hs gi|5868487|ref| gn 1 - 17547 17722 ex 2 3 CDSI 9.96 176 3284		CH.07_hs gi|5868487	1.3
335871	EOS35802	CH22_3246FG_629_19_LINK_EM:AC005500.GENSCAN.519-18		CH22_FGENES.629_19	1.3
303735	EOS03666	AA707750	Hs.202616	ESTs; Weakly similar to cis-Golgi matrix protein GM130 [R.norvegicus]	1.3
324048	EOS23979	AA378739		EST cluster (not in UniGene)	1.3
326720	EOS26651	c20_hs gi|6552456|ref| gn 1 + 84525 84677 ex 5 7 CDSI 11.78 153 1031		CH.20_hs gi|6552456	1.3
322309	EOS22240	AF086372		EST cluster (not in UniGene)	1.3
322136	EOS22067	AF075083		EST cluster (not in UniGene)	1.3
313460	EOS13391	AW028655	Hs.136033	ESTs	1.3
306275	EOS06206	AA936312		EST singleton (not in UniGene) with exon hit	1.3
321974	EOS21905	N76794		EST cluster (not in UniGene)	1.3
327600	EOS27531	c_3_hs gi|6004462|ref| gn 1 - 2621 2862 ex 1 4 CDSI -4.01 242 1407		CH.03_hs gi|6004462	1.3
329086	EOS29017	c_x_hs gi|5868604|ref| gn 1 - 35489 35588 ex 2 9 CDSI 2.55 100 719		CH.X_hs gi|5868604	1.3
336919	EOS36850	CH22_4690FG_346_6_		CH22_FGENES.346-6	1.3
302767	EOS02698	H94900	Hs.17882	ESTs	1.3
334786	EOS34717	CH22_2098FG_432_11_LINK_EM:AC005500.GENSCAN.293-14		CH22_FGENES.432_11	1.3
302472	EOS02403	AA317451	Hs.241451	SWI/SNF related; matrix associated; actin dependent regulator of chromatin; subfamily e; member 1	1.3
333033	EOS32964	CH22_259FG_68_8_LINK_EM:AC000097.GENSCAN.40-8		CH22_FGENES.68_8	1.3
330493	EOS30424	M27826	Hs.238380	Human endogenous retroviral protease mRNA; complete cds	1.3
330506	EOS30437	M61906	Hs.6241	phosphoinositide-3-kinase; regulatory subunit; polypeptide 1 (p85 alpha)	1.3
313932	EOS13863	AI147601	Hs.154087	ESTs	1.3
314394	EOS14325	AI380563	Hs.130816	ESTs	1.3
323033	EOS22964	AI744284	Hs.221727	ESTs	1.3
326431	EOS26362	c19_hs gi|5867371|ref| gn 1 + 15855 15971 ex 4 6 CDSI 7.79 117 1108		CH.19_hs gi|5867371	1.3
335547	EOS35478	CH22_2902FG_576_8_LINK_EM:AC005500.GENSCAN.467-8		CH22_FGENES.576_8	1.3
300548	EOS00479	AI026836	Hs.114689	ESTs	1.3
316504	EOS16435	AW135854	Hs.132458	ESTs	1.3
335756	EOS35687	CH22_3123FG_604_5_LINK_EM:AC005500.GENSCAN.493-10		CH22_FGENES.604_5	1.3
301209	EOS01140	AI809912	Hs.159354	ESTs	1.3
306610	EOS06541	AI000635		EST singleton (not in UniGene) with exon hit	1.3
314439	EOS14370	AI539443	Hs.137447	ESTs	1.3
315396	EOS15327	AW296107	Hs.152686	ESTs	1.3
335914	EOS35845	CH22_3291FG_636_10_LINK_EM:AC005500.GENSCAN.526-10		CH22_FGENES.636_10	1.3
333734	EOS33665	CH22_1000FG_260_2_LINK_EM:AC005500.GENSCAN.119-7		CH22_FGENES.260_2	1.3
312370	EOS12301	AA744692	Hs.166539	ESTs	1.3
304636	EOS04567	AA524031		EST singleton (not in UniGene) with exon hit	1.3
323166	EOS23097	AA291001		EST cluster (not in UniGene)	1.3
338702	EOS38633	CH22_7482FG__LINK_EM:AC005500.GENSCAN.480-1		CH22_EM:AC005500.GENSCAN.480-1	1.3
322331	EOS22262	AF086467		EST cluster (not in UniGene)	1.3
318706	EOS18637	AI383593	Hs.159148	ESTs	1.3
331186	EOS31117	T41159	Hs.8418	ESTs	1.3
334764	EOS34695	CH22_2076FG_428_13_LINK_EM:AC005500.GENSCAN.289-13		CH22_FGENES.428_13	1.3
327565	EOS27496	c_3_hs gi|5867811|ref| gn 1 + 32516 32778 ex 2 3 CDSI 0.20 263 368		CH.03_hs gi|5867811	1.3
335524	EOS35455	CH22_2879FG_572_4_LINK_EM:AC005500.GENSCAN.461-4		CH22_FGENES.572_4	1.3
308050	EOS07981	AI460004		EST singleton (not in UniGene) with exon hit	1.3
334172	EOS34103	CH22_1452FG_349_5_LINK_EM:AC005500.GENSCAN.208-6		CH22_FGENES.349_5	1.3
315674	EOS15605	AA651923	Hs.191850	ESTs	1.3
334876	EOS34807	CH22_2190FG_450_6_LINK_EM:AC005500.GENSCAN.339-6		CH22_FGENES.450_6	1.3
315606	EOS15537	AW298724	Hs.202639	ESTs	1.3
338779	EOS38710	CH22_7610FG__LINK_EM:AC005500.GENSCAN.526-15		CH22_EM:AC005500.GENSCAN.526-15	1.3
333511	EOS33442	CH22_766FG_171_5_LINK_EM:AC005500.GENSCAN.51-5		CH22_FGENES.171_5	1.3
329254	EOS29185	c_x_hs gi|5868733|ref| gn 1 + 4133 4214 ex 1 2 CDSI -0.36 82 2833		CH.X_hs gi|5868733	1.3
319510	EOS19441	W88633	Hs.254562	ESTs	1.3
339418	EOS39349	CH22_8411FG__LINK_DJ579N16.GENSCAN.11-4		CH22_DJ579N16.GENSCAN.11-4	1.3
321012	EOS20943	AA737314		EST cluster (not in UniGene)	1.3

333217	EOS33148	CH22_454FG_104_9_LINK_EM:AC000097.GENSCAN.108-8		CH22_FGENES.104_9	1.3
338561	EOS38492	CH22_7294FG__LINK_EM:AC005500.GENSCAN.421-5		CH22_EM:AC005500.GENSCAN.421-5	1.3
335742	EOS35673	CH22_3105FG_601_13_LINK_EM:AC005500.GENSCAN.491-14		CH22_FGENES.601_13	1.3
334993	EOS34924	CH22_2314FG_469_14_LINK_EM:AC005500.GENSCAN.365-16		CH22_FGENES.469_14	1.3
323430	EOS23361	AW062479		EST cluster (not in UniGene)	1.3
306069	EOS06000	AA906983		EST singleton (not in UniGene) with exon hit	1.3
331681	EOS31612	W85712	Hs.119571	collagen; type III; alpha 1 (Ehlers-Danlos syndrome type IV; autosomal dominant)	1.3
337986	EOS37917	CH22_6441FG__LINK_EM:AC005500.GENSCAN.110-7		CH22_EM:AC005500.GENSCAN.110-7	1.3
313204	EOS13135	AI800518	Hs.118158	ESTs	1.3
323189	EOS23120	AL121194	Hs.120589	ESTs	1.3
318171	EOS18102	AA381202		EST cluster (not in UniGene)	1.3
307156	EOS07087	AI186762		EST singleton (not in UniGene) with exon hit	1.3
332713	EOS32644	AA349792	Hs.78489	mutY (E. coli) homolog	1.3
312828	EOS12759	AI865455	Hs.211818	ESTs; Moderately similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.3
301127	EOS01058	AA758109	Hs.121072	ESTs	1.3
311260	EOS11191	AI672509	Hs.196582	ESTs	1.3
338364	EOS38295	CH22_7007FG__LINK_EM:AC005500.GENSCAN.323-7		CH22_EM:AC005500.GENSCAN.323-7	1.3
337904	EOS37835	CH22_6318FG__LINK_EM:AC005500.GENSCAN.56-17		CH22_EM:AC005500.GENSCAN.56-17	1.3
329347	EOS29278	c_x_hs gi|6456785|ref| gn 1 + 18433 18897 ex 4 4 CDSl 43.39 465 3718		CH.X_hs gi|6456785	1.3
313329	EOS13260	AW293704	Hs.122658	ESTs	1.3
314367	EOS14298	AA535749		EST cluster (not in UniGene)	1.3
317098	EOS17029	AI123513	Hs.125456	ESTs	1.3
306462	EOS06393	AA983397		EST singleton (not in UniGene) with exon hit	1.3
301254	EOS01185	AI049624		EST cluster (not in UniGene) with exon hit	1.3
335504	EOS35435	CH22_2856FG_571_15_LINK_EM:AC005500.GENSCAN.460-34		CH22_FGENES.571_15	1.3
334270	EOS34201	CH22_1559FG_368_2_LINK_EM:AC005500.GENSCAN.228-3		CH22_FGENES.368_2	1.3
334324	EOS34255	CH22_1616FG_375_1_LINK_EM:AC005500.GENSCAN.235-1		CH22_FGENES.375_1	1.3
304254	EOS04185	AA046273	Hs.111334	ferritin; light polypeptide	1.3
305731	EOS05662	AA829363		EST singleton (not in UniGene) with exon hit	1.3
323284	EOS23215	AA279381	Hs.190010	ESTs	1.3
322007	EOS21938	AW410646	Hs.165739	ESTs	1.3
334537	EOS34468	CH22_1839FG_403_2_LINK_EM:AC005500.GENSCAN.268-2		CH22_FGENES.403_2	1.3
302360	EOS02291	AJ010901	Hs.198267	mucin 4; tracheobronchial	1.3
311641	EOS11572	AI948829	Hs.213786	ESTs	1.3
324643	EOS24574	AI436356	Hs.130729	ESTs	1.3
327554	EOS27485	c_3_hs gi|5867801|ref| gn 2 - 23092 23191 ex 2 6 CDSi 10.44 100 107		CH.03_hs gi|5867801	1.3
312165	EOS12096	AW292139	Hs.115789	ESTs	1.3
304679	EOS04610	AA548741		EST singleton (not in UniGene) with exon hit	1.3
319564	EOS19495	AA026777	Hs.169732	ESTs	1.3
310860	EOS10791	AW015920	Hs.161359	ESTs	1.3
337161	EOS37092	CH22_5180FG_561_3_		CH22_FGENES.561-3	1.3
311155	EOS11086	AI634410	Hs.197608	EST	1.3
336846	EOS36777	CH22_4540FG_263_5_		CH22_FGENES.263-5	1.3
310985	EOS10916	T51842		EST cluster (not in UniGene)	1.3
329499	EOS29430	c10_p2 gi|3983518|gb|A gn 5 + 33463 33789 ex 1 1 CDSo 34.50 327 97		CH.10_p2 gi|3983518	1.3
334924	EOS34855	CH22_2244FG_459_2_LINK_EM:AC005500.GENSCAN.351-2		CH22_FGENES.459_2	1.3
330861	EOS30792	AA084064	Hs.185747	ESTs	1.3
324658	EOS24589	AI694767	Hs.129179	ESTs	1.3
323362	EOS23293	AL135067	Hs.117182	ESTs	1.3
330468	EOS30399	L10343	Hs.112341	protease inhibitor 3; skin-derived (SKALP)	1.3
314198	EOS14129	AA897581	Hs.128773	ESTs	1.3
339436	EOS39367	CH22_8431FG__LINK_DJ579N16.GENSCAN.19-1		CH22_DJ579N16.GENSCAN.19-1	1.3
312483	EOS12414	AI417526	Hs.184636	ESTs	1.3
321505	EOS21436	H73183	Hs.129885	ESTs	1.3
332254	EOS32185	N64702	Hs.194140	ESTs	1.3
328253	EOS28184	c_6_hs gi|6381894|ref| gn 1 - 4411 4509 ex 1 5 CDSI 4.20 99 4561		CH.06_hs gi|6381894	1.3
332357	EOS32288	W73417	Hs.103183	EST	1.3
329017	EOS28948	c_x_hs gi|6682532|ref| gn 7 - 255591 255672 ex 3 3 CDSf 12.94 82 22		CH.X_hs gi|6682532	1.3
337504	EOS37435	CH22_5739FG_803_2_		CH22_FGENES.803-2	1.3
316625	EOS16556	AA780307	Hs.122156	ESTs	1.3
335389	EOS35320	CH22_2739FG_545_1_LINK_EM:AC005500.GENSCAN.436-1		CH22_FGENES.545_1	1.3
310017	EOS09948	AI188739	Hs.148488	ESTs	1.3
314354	EOS14285	AL037984	Hs.208982	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.3
324641	EOS24572	AI732515	Hs.189218	ESTs	1.3
335207	EOS35138	CH22_2546FG_510_4_LINK_EM:AC005500.GENSCAN.402-3		CH22_FGENES.510_4	1.3
333673	EOS33604	CH22_934FG_246_5_LINK_EM:AC005500.GENSCAN.101-3			

				CH22_FGENES.246_5	1.3
334370	EOS34301	CH22_1664FG_378_18_LINK_EM:AC005500.GENSCAN.240-1			
				CH22_FGENES.378_18	1.3
328690	EOS28621	c_7_hs gi|6588001|ref| gn 7 - 571207 571274 ex 1 3 CDSI 3.34 68 4325			
				CH.07_hs gi|6588001	1.3
323208	EOS23139	AA203415	Hs.136200	ESTs	1.3
307010	EOS06941	AI140014		EST singleton (not in UniGene) with exon hit	1.3
316563	EOS16494	AI587083	Hs.200558	ESTs; Weakly similar to !!!! ALU SUBFAMILY SP WARNING ENTRY !!!! [H.sapiens]	1.3
312219	EOS12150	H73505	Hs.117874	ESTs	1.3
319884	EOS19815	T73234		EST cluster (not in UniGene)	1.3
334720	EOS34651	CH22_2030FG_421_31_LINK_EM:AC005500.GENSCAN.282-31			
				CH22_FGENES.421_31	1.3
335836	EOS35767	CH22_3210FG_621_3_LINK_EM:AC005500.GENSCAN.513-3			
				CH22_FGENES.621_3	1.3
305448	EOS05379	AA737894	Hs.29797	ribosomal protein L10	1.3
314885	EOS14816	AI049878	Hs.133032	ESTs	1.3
320130	EOS20061	AI820675	Hs.203804	ESTs	1.3
310567	EOS10498	AI691065	Hs.155780	ESTs	1.3
323898	EOS23829	AA347566		EST cluster (not in UniGene)	1.3
336132	EOS36063	CH22_3522FG_703_2_LINK_DA59H18.GENSCAN.9-2			
				CH22_FGENES.703_2	1.3
337958	EOS37889	CH22_6403FG__LINK_EM:AC005500.GENSCAN.98-6			
				CH22_EM:AC005500.GENSCAN.98-6	1.3
305630	EOS05561	AA804508		EST singleton (not in UniGene) with exon hit	1.3
334916	EOS34847	CH22_2235FG_457_7_LINK_EM:AC005500.GENSCAN.347-1			
				CH22_FGENES.457_7	1.3
333542	EOS33473	CH22_799FG_178_4_LINK_EM:AC005500.GENSCAN.59-4			
				CH22_FGENES.178_4	1.3
331151	EOS31082	R82331	Hs.164599	ESTs	1.3
315095	EOS15026	AA831815	Hs.243788	ESTs	1.3
331593	EOS31524	N72150	Hs.50193	EST	1.3
323767	EOS23698	AI807408	Hs.166368	ESTs	1.3
334561	EOS34492	CH22_1865FG_405_1_LINK_EM:AC005500.GENSCAN.270-5			
				CH22_FGENES.405_1	1.3
308191	EOS08122	AI538878		EST singleton (not in UniGene) with exon hit	1.3
319571	EOS19502	N91399	Hs.220826	ESTs	1.3
316200	EOS16131	AI914535	Hs.221377	ESTs	1.3
305996	EOS05927	AA889338	Hs.163356	EST	1.2
318055	EOS17986	AI249193	Hs.145945	ESTs	1.2
315570	EOS15501	AI860360	Hs.160316	ESTs	1.2
320792	EOS20723	AW236504	Hs.247020	ESTs	1.2
331649	EOS31580	W20364	Hs.55412	ESTs; Weakly similar to c29 [M.musculus]	1.2
303839	EOS03770	Z45939		EST cluster (not in UniGene) with exon hit	1.2
324399	EOS24330	AA814768	Hs.21396	ESTs	1.2
317172	EOS17103	AI741232	Hs.206744	ESTs	1.2
312452	EOS12383	AI692643	Hs.172749	ESTs	1.2
325482	EOS25413	c12_hs gi|5866957|ref| gn 3 + 47957 48078 ex 5 7 CDSi 10.25 122 1896			
				CH.12_hs gi|5866957	1.2
311395	EOS11326	R23313		EST cluster (not in UniGene)	1.2
336124	EOS36055	CH22_3513FG_701_9_LINK_DA59H18.GENSCAN.8-9			
				CH22_FGENES.701_9	1.2
320082	EOS20013	AA487678	Hs.189738	ESTs	1.2
312168	EOS12099	T92251	Hs.198882	ESTs	1.2
338000	EOS37931	CH22_6472FG__LINK_EM:AC005500.GENSCAN.119-5			
				CH22_EM:AC005500.GENSCAN.119-5	1.2
338852	EOS38783	CH22_7705FG__LINK_DJ246D7.GENSCAN.12-1			
				CH22_DJ246D7.GENSCAN.12-1	1.2
312090	EOS12021	N57692	Hs.118064	ESTs	1.2
316480	EOS16411	AI749921	Hs.205377	ESTs	1.2
333259	EOS33190	CH22_500FG_118_7_LINK_EM:AC005500.GENSCAN.2-7			
				CH22_FGENES.118_7	1.2
335211	EOS35142	CH22_2550FG_511_2_LINK_EM:AC005500.GENSCAN.403-2			
				CH22_FGENES.511_2	1.2
321950	EOS21881	AA594780	Hs.172318	ESTs	1.2
337937	EOS37868	CH22_6370FG__LINK_EM:AC005500.GENSCAN.86-1			
				CH22_EM:AC005500.GENSCAN.86-1	1.2
316576	EOS16507	AI732114	Hs.193046	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.2
322770	EOS22701	AA045796	Hs.159971	SWI/SNF related; matrix associated; actin dependent regulator of chromatin; subfamily b; member 1	1.2
329369	EOS29300	c_x_hs gi|5868842|ref| gn 1 - 121148 121516 ex 3 4 CDSI 8.50 369 3910			
				CH.X_hs gi|5868842	1.2
304183	EOS04114	H91161		EST singleton (not in UniGene) with exon hit	1.2
339370	EOS39301	CH22_8343FG__LINK_BA232E17.GENSCAN.1-12			
				CH22_BA232E17.GENSCAN.1-12	1.2
303941	EOS03872	AW473878	Hs.156110	Immunoglobulin kappa variable 1D-8	1.2
302245	EOS02176	H18835		EST cluster (not in UniGene) with exon hit	1.2
335255	EOS35186	CH22_2597FG_517_2_LINK_EM:AC005500.GENSCAN.411-2			
				CH22_FGENES.517_2	1.2
316610	EOS16541	AW087973	Hs.126731	ESTs	1.2
314915	EOS14846	AA573072	Hs.187748	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.2
315426	EOS15357	AI391486	Hs.128171	ESTs	1.2
334003	EOS33934	CH22_1281FG_310_28_LINK_EM:AC005500.GENSCAN.167-27			
				CH22_FGENES.310_28	1.2
304350	EOS04281	AA186871		EST singleton (not in UniGene) with exon hit	1.2
325173	EOS25104	AI133215	Hs.144662	ESTs; Moderately similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.2
312313	EOS12244	AW293341	Hs.122505	ESTs	1.2
333366	EOS33297	CH22_612FG_142_3_LINK_EM:AC005500.GENSCAN.22-6			

				CH22_FGENES.142_3	1.2
334970	EOS34901	CH22_2291FG_466_3_LINK_EM:AC005500.GENSCAN.361-2		CH22_FGENES.466_3	1.2
338668	EOS38599	CH22_7441FG__LINK_EM:AC005500.GENSCAN.465-1		CH22_EM:AC005500.GENSCAN.465-1	1.2
336502	EOS36433	CH22_3926FG_833_8_LINK_DJ579N16.GENSCAN.5-9		CH22_FGENES.833_8	1.2
309438	EOS09369	AW102802	Hs.225787	ESTs; Moderately similar to hypothetical protein [H.sapiens]	1.2
336194	EOS36125	CH22_3591FG_717_20_LINK_DA59H18.GENSCAN.20-19		CH22_FGENES.717_20	1.2
336678	EOS36609	CH22_4156FG_43_6_		CH22_FGENES.43-6	1.2
321401	EOS21332	W90406	Hs.35962	ESTs	1.2
306026	EOS05957	AA902309		EST singleton (not in UniGene) with exon hit	1.2
336434	EOS36365	CH22_3854FG_826_1_LINK_BA232E17.GENSCAN.8-1		CH22_FGENES.826_1	1.2
315257	EOS15188	AW157431	Hs.248941	ESTs	1.2
328349	EOS28280	c_7_hs gi|5868383|ref| gn 7 - 260704 260804 ex 2 9 CDSI 4.37 101 621		CH.07_hs gi|5868383	1.2
326112	EOS26043	c17_hs gi|5867192|ref| gn 1 + 2151 2725 ex 1 1 CDSI 54.87 575 1272		CH.17_hs gi|5867192	1.2
333995	EOS33926	CH22_1272FG_310_19_LINK_EM:AC005500.GENSCAN.167-18		CH22_FGENES.310_19	1.2
323683	EOS23614	AI380045	Hs.225033	ESTs	1.2
330143	EOS30074	c21_p2 gi|4210430|emb| gn 3 + 184737 184848 ex 4 4 CDSI 1.71 112 111		CH.21_p2 gi|4210430	1.2
329789	EOS29720	c14_p2 gi|6469354|emb| gn 2 - 118977 119036 ex 1 3 CDSI 1.19 60 1517		CH.14_p2 gi|6469354	1.2
324397	EOS24328	AA307836	Hs.118758	ESTs; Weakly similar to RLF [H.sapiens]	1.2
308729	EOS08660	AI799766	Hs.208627	EST	1.2
323939	EOS23870	AW499632	Hs.115696	ESTs	1.2
333444	EOS33375	CH22_694FG_153_1_LINK_EM:AC005500.GENSCAN.34-1		CH22_FGENES.153_1	1.2
306302	EOS06233	AA937901		EST singleton (not in UniGene) with exon hit	1.2
313693	EOS13624	AW469180	Hs.170651	ESTs	1.2
316652	EOS16583	AA789249		EST cluster (not in UniGene)	1.2
332325	EOS32256	T79428	Hs.191264	ESTs	1.2
336235	EOS36166	CH22_3633FG_740_2_LINK_DA59H18.GENSCAN.44-2		CH22_FGENES.740_2	1.2
319436	EOS19367	R02750		EST cluster (not in UniGene)	1.2
312335	EOS12266	AW043620	Hs.236993	ESTs	1.2
322109	EOS22040	AI884327	Hs.244737	ESTs	1.2
328466	EOS28397	c_7_hs gi|5868434|ref| gn 1 - 15643 15900 ex 1 2 CDSI 2.36 258 1608		CH.07_hs gi|5868434	1.2
323244	EOS23175	T70731		EST cluster (not in UniGene)	1.2
312510	EOS12441	AA779907	Hs.117558	ESTs	1.2
314853	EOS14784	AA729232	Hs.153279	ESTs	1.2
336946	EOS36877	CH22_4731FG_355_2_		CH22_FGENES.355-2	1.2
303874	EOS03805	AA258921		EST cluster (not in UniGene) with exon hit	1.2
312658	EOS12589	AA730280	Hs.120936	ESTs	1.2
308354	EOS08285	AI611044		EST singleton (not in UniGene) with exon hit	1.2
310073	EOS10004	AI335004	Hs.148558	ESTs	1.2
324777	EOS24708	AA744046	Hs.133350	ESTs	1.2
300897	EOS00828	AI890356	Hs.127804	ESTs	1.2
308371	EOS08302	AI620666	Hs.242510	EST	1.2
306358	EOS06289	AA961821		EST singleton (not in UniGene) with exon hit	1.2
312295	EOS12226	AA578233	Hs.173863	ESTs	1.2
319792	EOS19723	R20317	Hs.22968	ESTs	1.2
338546	EOS38477	CH22_7267FG__LINK_EM:AC005500.GENSCAN.410-1		CH22_EM:AC005500.GENSCAN.410-1	1.2
314546	EOS14477	AW007211	Hs.186672	ESTs	1.2
338494	EOS38425	CH22_7184FG__LINK_EM:AC005500.GENSCAN.385-5		CH22_EM:AC005500.GENSCAN.385-5	1.2
331131	EOS31062	R54797	Hs.26238	EST; Weakly similar to reverse transcriptase homolog [H.sapiens]	1.2
309939	EOS09870	AW419122		EST singleton (not in UniGene) with exon hit	1.2
332932	EOS32863	CH22_153FG_38_6_LINK_C20H12.GENSCAN.29-6		CH22_FGENES.38_6	1.2
309653	EOS09584	AW196800	Hs.180842	ribosomal protein L13	1.2
318647	EOS18578	AI526152		EST cluster (not in UniGene)	1.2
304044	EOS03975	T52479	Hs.252259	ribosomal protein S3	1.2
330307	EOS30238	c_7_p2 gi|4877982|gb|A gn 2 + 107384 107559 ex 2 4 CDSI 9.96 176 4		CH.07_p2 gi|4877982	1.2
314499	EOS14430	AL044570	Hs.147975	ESTs	1.2
338053	EOS37984	CH22_6552FG__LINK_EM:AC005500.GENSCAN.158-1		CH22_EM:AC005500.GENSCAN.158-1	1.2
332991	EOS32922	CH22_215FG_56_4_LINK_EM:AC000097.GENSCAN.17-4		CH22_FGENES.56_4	1.2
306308	EOS06239	AA946870		EST singleton (not in UniGene) with exon hit	1.2
338120	EOS38051	CH22_6655FG__LINK_EM:AC005500.GENSCAN.195-1		CH22_EM:AC005500.GENSCAN.195-1	1.2
313703	EOS13634	AI161293	Hs.146862	ESTs; Weakly similar to KIAA0525 protein [H.sapiens]	1.2
330563	EOS30494	U50553	Hs.147916	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 3	1.2
332886	EOS32817	CH22_106FG_33_7_LINK_C20H12.GENSCAN.22-9		CH22_FGENES.33_7	1.2
303844	EOS03775	U94362	Hs.58589	glycogenin 2	1.2
321755	EOS21686	AI215881	Hs.144042	ESTs	1.2
333532	EOS33463	CH22_789FG_175_19_LINK_EM:AC005500.GENSCAN.53-25			

				CH22_FGENES.175_19	1.2
332863	EOS32794	CH22_81FG_28_3_LINK_C20H12.GENSCAN.18-3			
				CH22_FGENES.28_3	1.2
333254	EOS33185	CH22_495FG_118_2_LINK_EM:AC005500.GENSCAN.2-2			
				CH22_FGENES.118_2	1.2
317459	EOS17390	AI367254	Hs.131248	ESTs	1.2
315353	EOS15284	AW452608	Hs.129817	ESTs	1.2
300732	EOS00663	AI369956	Hs.257891	ESTs	1.2
303502	EOS03433	AA488528		EST cluster (not in UniGene) with exon hit	1.2
333126	EOS33057	CH22_355FG_82_3_LINK_EM:AC000097.GENSCAN.66-10			
				CH22_FGENES.82_3	1.2
332929	EOS32860	CH22_150FG_38_3_LINK_C20H12.GENSCAN.29-3			
				CH22_FGENES.38_3	1.2
329502	EOS29433	c10_p2 gi|3983517|gb|U gn 1 + 75 338 ex 1 1 CDSo 46.82 264 100			
				CH.10_p2 gi|3983517	1.2
333408	EOS33339	CH22_657FG_145_6_LINK_EM:AC005500.GENSCAN.26-6			
				CH22_FGENES.145_6	1.2
315472	EOS15403	AA828850	Hs.165469	ESTs	1.2
328290	EOS28221	c_7_hs gi|5868363|ref| gn 2 - 127366 127496 ex 1 5 CDSi 5.24 131 289			
				CH.07_hs gi|5868363	1.2
328662	EOS28593	c_7_hs gi|6004473|ref| gn 22 + 1184773 1184855 ex 7 8 CDSi 12.72 83 3916			
				CH.07_hs gi|6004473	1.2
319808	EOS19739	T58960		EST cluster (not in UniGene)	1.2
303929	EOS03860	AW470753		EST singleton (not in UniGene) with exon hit	1.2
315712	EOS15643	AI950133	Hs.120882	ESTs; Moderately similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.2
307391	EOS07322	AI225058		EST singleton (not in UniGene) with exon hit	1.2
335499	EOS35430	CH22_2851FG_571_8_LINK_EM:AC005500.GENSCAN.460-28			
				CH22_FGENES.571_8	1.2
303792	EOS03723	C75094	Hs.199839	ESTs; Highly similar to NG22 [H.sapiens]	1.2
327287	EOS27218	c_1_hs gi|5867479|ref| gn 1 - 62838 63024 ex 4 5 CDSi 11.66 187 1628			
				CH.01_hs gi|5867479	1.2
317713	EOS17644	AI733306	Hs.128071	ESTs	1.2
330137	EOS30068	c21_p2 gi|4210430|emb| gn 1 - 21220 21377 ex 2 3 CDSi 1.89 158 104			
				CH.21_p2 gi|4210430	1.2
308157	EOS08088	AI510824	Hs.75968	thymosin; beta 4; X chromosome	1.2
314452	EOS14383	AL042699	Hs.209222	ESTs	1.2
308268	EOS08199	AI567509	Hs.172928	collagen; type I; alpha 1	1.2
321467	EOS21398	X13075		EST cluster (not in UniGene)	1.2
320993	EOS20924	AL050145	Hs.225986	Homo sapiens mRNA; cDNA DKFZp586C2020 (from clone DKFZp586C2020)	1.2
336778	EOS36709	CH22_4367FG_159_4_		CH22_FGENES.159-4	1.2
319827	EOS19758	T62778		EST cluster (not in UniGene)	1.2
308249	EOS08180	AI560998		EST singleton (not in UniGene) with exon hit	1.2
310094	EOS10025	AW450967	Hs.235240	ESTs	1.2
336902	EOS36833	CH22_4655FG_331_2_		CH22_FGENES.331-2	1.2
339044	EOS38975	CH22_7944FG__LINK_DA59H18.GENSCAN.27-5			
				CH22_DA59H18.GENSCAN.27-5	1.2
336675	EOS36606	CH22_4153FG_43_3_		CH22_FGENES.43-3	1.2
303563	EOS03494	AA367699	Hs.118787	transforming growth factor; beta-induced; 68kD	1.2
330673	EOS30604	D57823	Hs.92962	Sec23 (S. cerevisiae) homolog A	1.2
311814	EOS11745	AW377113	Hs.119640	ESTs; Moderately similar to zinc finger protein [H.sapiens]	1.2
335481	EOS35412	CH22_2833FG_570_10_LINK_EM:AC005500.GENSCAN.460-4			
				CH22_FGENES.570_10	1.2
314775	EOS14706	AI149880	Hs.188809	ESTs	1.2
324961	EOS24892	AA613792		EST cluster (not in UniGene)	1.2
313458	EOS13389	AA007259	Hs.255853	ESTs	1.2
307074	EOS07005	AI150989		EST singleton (not in UniGene) with exon hit	1.2
337964	EOS37895	CH22_6410FG__LINK_EM:AC005500.GENSCAN.100-9			
				CH22_EM:AC005500.GENSCAN.100-9	1.2
326519	EOS26450	c19_hs gi|5867439|ref| gn 4 + 166004 166243 ex 4 5 CDSi 4.49 240 2534			
				CH.19_hs gi|5867439	1.2
337366	EOS37297	CH22_5551FG_736_1_		CH22_FGENES.736-1	1.2
322340	EOS22271	AF088076		EST cluster (not in UniGene)	1.2
307954	EOS07885	AI419692		EST singleton (not in UniGene) with exon hit	1.2
328615	EOS28546	c_7_hs gi|5868239|ref| gn 2 + 35214 35347 ex 3 4 CDSi 11.49 134 3651			
				CH.07_hs gi|5868239	1.2
317787	EOS17718	AW339612	Hs.249364	ESTs	1.2
335288	EOS35219	CH22_2630FG_527_1_LINK_EM:AC005500.GENSCAN.421-1			
				CH22_FGENES.527_1	1.2
323175	EOS23106	AI827137	Hs.184023	ESTs	1.2
330893	EOS30824	AA149620	Hs.71999	ESTs	1.2
306810	EOS06741	AI057294		EST singleton (not in UniGene) with exon hit	1.2
338239	EOS38170	CH22_6833FG__LINK_EM:AC005500.GENSCAN.264-5			
				CH22_EM:AC005500.GENSCAN.264-5	1.2
332347	EOS32278	W60326	Hs.221716	ESTs	1.2
309782	EOS09713	AW275156	Hs.156110	Immunoglobulin kappa variable 1D-8	1.2
322518	EOS22449	AI133446		EST cluster (not in UniGene)	1.2
301187	EOS01118	AA806542		EST cluster (not in UniGene) with exon hit	1.2
312129	EOS12060	AW300867		EST cluster (not in UniGene)	1.2
334714	EOS34645	CH22_2024FG_421_25_LINK_EM:AC005500.GENSCAN.282-25			
				CH22_FGENES.421_25	1.2
316586	EOS16517	AI205077	Hs.144689	ESTs	1.2
320488	EOS20419	R31386		EST cluster (not in UniGene)	1.2
327458	EOS27389	c_2_hs gi|6004455|ref| gn 3 + 173257 173378 ex 5 7 CDSi 4.03 122 1184			
				CH.02_hs gi|6004455	1.2
336707	EOS36638	CH22_4212FG_64_3_		CH22_FGENES.64-3	1.2
313561	EOS13492	AA040155		EST cluster (not in UniGene)	1.2

330906	EOS30837	AA169498	Hs.72804	ESTs	1.2
330987	EOS30918	H40988	Hs.131965	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.2
325041	EOS24972	AI809182	Hs.130907	ESTs	1.2
313225	EOS13156	AA502384	Hs.151529	ESTs	1.2
305295	EOS05226	AA687131		EST singleton (not in UniGene) with exon hit	1.2
306896	EOS06827	AI093383		EST singleton (not in UniGene) with exon hit	1.2
326981	EOS26912	c21_hs gi|6588016|ref| gn 3 + 105091 106038 ex 1 1 CDSo 122.69 948 567		CH.21_hs gi|6588016	1.2
332225	EOS32156	N33213	Hs.100425	ESTs	1.2
318802	EOS18733	R19443	Hs.92414	ESTs	1.2
318413	EOS18344	AI138592	Hs.144936	ESTs	1.2
312292	EOS12223	AW451893	Hs.151124	ESTs	1.2
323753	EOS23684	AA327102		EST cluster (not in UniGene)	1.2
313582	EOS13513	AW207684	Hs.13583	ESTs	1.2
317836	EOS17767	AA983913	Hs.128929	ESTs	1.2
332868	EOS32799	CH22_86FG_28_8_LINK_C20H12.GENSCAN.18-8		CH22_FGENES.28_8	1.2
336924	EOS36855	CH22_4699FG_347_9_		CH22_FGENES.347-9	1.2
327791	EOS27722	c_5_hs gi|5867977|ref| gn 1 + 22491 22610 ex 6 7 CDSl 11.29 120 658		CH.05_hs gi|5867977	1.2
330717	EOS30648	AA233926	Hs.23635	ESTs	1.2
322944	EOS22875	AA112573		EST cluster (not in UniGene)	1.2
312108	EOS12039	T82331	Hs.127453	ESTs	1.2
332570	EOS32501	AA401376	Hs.26176	ESTs	1.2
330880	EOS30811	AA132420	Hs.53542	KIAA0986 protein	1.2
310341	EOS10272	AW302773		EST cluster (not in UniGene)	1.2
334012	EOS33943	CH22_1290FG_313_3_LINK_EM:AC005500.GENSCAN.169-3		CH22_FGENES.313_3	1.2
318230	EOS18161	AA558125		EST cluster (not in UniGene)	1.2
336071	EOS36002	CH22_3457FG_685_3_LINK_DJ32I10.GENSCAN.21-6		CH22_FGENES.685_3	1.2
338510	EOS38441	CH22_7208FG__LINK_EM:AC005500.GENSCAN.391-22		CH22_EM:AC005500.GENSCAN.391-22	1.2
334487	EOS34418	CH22_1786FG_395_9_LINK_EM:AC005500.GENSCAN.258-10		CH22_FGENES.395_9	1.2
320661	EOS20592	AA864846		EST cluster (not in UniGene)	1.2
335200	EOS35131	CH22_2538FG_508_9_LINK_EM:AC005500.GENSCAN.401-9		CH22_FGENES.508_9	1.2
333582	EOS33513	CH22_842FG_201_2_LINK_EM:AC005500.GENSCAN.72-3		CH22_FGENES.201_2	1.2
320789	EOS20720	R78712		EST cluster (not in UniGene)	1.2
321185	EOS21116	H51659	Hs.189854	ESTs	1.2
337740	EOS37671	CH22_6085FG__LINK_EM:AC000097.GENSCAN.100-6		CH22_EM:AC000097.GENSCAN.100-6	1.2
315064	EOS14995	AA775208	Hs.136423	ESTs	1.2
334883	EOS34814	CH22_2197FG_451_6_LINK_EM:AC005500.GENSCAN.340-6		CH22_FGENES.451_6	1.2
331825	EOS31756	AA411144	Hs.104768	ESTs	1.2
319141	EOS19072	F12377		EST cluster (not in UniGene)	1.1
333682	EOS33613	CH22_944FG_247_10_LINK_EM:AC005500.GENSCAN.102-10		CH22_FGENES.247_10	1.1
336140	EOS36071	CH22_3530FG_705_2_LINK_DA59H18.GENSCAN.10-2		CH22_FGENES.705_2	1.1
320727	EOS20658	U96044		EST cluster (not in UniGene)	1.1
323947	EOS23878	AA649842	Hs.186667	ESTs	1.1
324746	EOS24677	AA603367	Hs.222294	ESTs	1.1
306744	EOS06675	AI031882		EST singleton (not in UniGene) with exon hit	1.1
326517	EOS26448	c19_hs gi|5867439|ref| gn 1 + 44732 46356 ex 6 6 CDSl 148.22 1625 2512		CH.19_hs gi|5867439	1.1
333597	EOS33528	CH22_858FG_211_5_LINK_EM:AC005500.GENSCAN.79-5		CH22_FGENES.211_5	1.1
330135	EOS30066	c21_p2 gi|4456470|emb| gn 2 - 121583 121885 ex 2 2 CDSf 18.67 303 102		CH.21_p2 gi|4456470	1.1
315118	EOS15049	AA564921	Hs.143899	ESTs	1.1
302893	EOS02824	AL117539	Hs.173515	Homo sapiens mRNA; cDNA DKFZp586H021 (from clone DKFZp586H021)	1.1
337169	EOS37100	CH22_5189FG_563_1_		CH22_FGENES.563-1	1.1
336121	EOS36052	CH22_3510FG_701_6_LINK_DA59H18.GENSCAN.8-6		CH22_FGENES.701_6	1.1
323332	EOS23263	AI829520	Hs.227513	ESTs	1.1
320911	EOS20842	AI056872	Hs.133386	ESTs	1.1
327990	EOS27921	c_6_hs gi|5868218|ref| gn 2 - 36225 36503 ex 1 2 CDSl 16.35 279 1419		CH.06_hs gi|5868218	1.1
320425	EOS20356	C14069	Hs.201627	ESTs; Moderately similar to !!!! ALU SUBFAMILY SQ WARNING ENTRY !!!! [H.sapiens]	1.1
327075	EOS27006	c21_hs gi|6531965|ref| gn 58 + 4041318 4041431 ex 4 4 CDSl 1.79 114 1285		CH.21_hs gi|6531965	1.1
314384	EOS14315	AA535840	Hs.162203	ESTs; Weakly similar to alternatively spliced product using exon 13A [H.sapiens]	1.1
338716	EOS38647	CH22_7502FG__LINK_EM:AC005500.GENSCAN.488-9		CH22_EM:AC005500.GENSCAN.488-9	1.1
330886	EOS30817	AA135606	Hs.189384	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.1
327331	EOS27262	c_1_hs gi|5867516|ref| gn 4 - 55606 55737 ex 2 6 CDSl 7.01 132 2349		CH.01_hs gi|5867516	1.1
326714	EOS26645	c20_hs gi|5867595|ref| gn 2 + 124490 124568 ex 5 6 CDSl 0.11 79 1020		CH.20_hs gi|5867595	1.1
316734	EOS16665	AW080237	Hs.252884	ESTs	1.1
311660	EOS11591	AI978583	Hs.232161	ESTs	1.1
312757	EOS12688	AI285970	Hs.183817	ESTs	1.1

331686	EOS31617	W88502	Hs.182258	ESTs	1.1
337840	EOS37771	CH22_6223FG__LINK_EM:AC005500.GENSCAN.26-9		CH22_EM:AC005500.GENSCAN.26-9	1.1
332093	EOS32024	AA608794	Hs.112592	ESTs	1.1
319595	EOS19526	H81361	Hs.194485	ESTs	1.1
315990	EOS15921	AI800041	Hs.190555	ESTs	1.1
322438	EOS22369	W44531	Hs.167851	ESTs	1.1
332965	EOS32896	CH22_189FG_50_3_LINK_EM:AC000097.GENSCAN.3-5		CH22_FGENES.50_3	1.1
337182	EOS37113	CH22_5204FG_570_2_		CH22_FGENES.570-2	1.1
334948	EOS34879	CH22_2269FG_465_15_LINK_EM:AC005500.GENSCAN.359-13		CH22_FGENES.465_15	1.1
325864	EOS25795	c16_hs gi|5867069|ref| gn 2 - 110834 110904 ex 3 3 CDSf 9.76 71 457		CH.16_hs gi|5867069	1.1
337760	EOS37691	CH22_6110FG__LINK_EM:AC000097.GENSCAN.116-8		CH22_EM:AC000097.GENSCAN.116-8	1.1
315422	EOS15353	AW135357	Hs.192374	ESTs	1.1
338889	EOS38820	CH22_7746FG__LINK_DJ32I10.GENSCAN.7-1		CH22_DJ32I10.GENSCAN.7-1	1.1
332961	EOS32892	CH22_185FG_48_18_LINK_EM:AC000097.GENSCAN.2-14		CH22_FGENES.48_18	1.1
314703	EOS14634	AI791249		EST cluster (not in UniGene)	1.1
317791	EOS17722	AI801500	Hs.128457	ESTs	1.1
333680	EOS33611	CH22_942FG_247_7_LINK_EM:AC005500.GENSCAN.102-7		CH22_FGENES.247_7	1.1
322419	EOS22350	AA248987	Hs.14084	ESTs; Highly similar to zinc RING finger protein SAG [M.musculus]	1.1
338124	EOS38055	CH22_6661FG__LINK_EM:AC005500.GENSCAN.196-2		CH22_EM:AC005500.GENSCAN.196-2	1.1
308884	EOS08815	AI833131	Hs.179100	ESTs	1.1
333349	EOS33280	CH22_595FG_140_3_LINK_EM:AC005500.GENSCAN.20-3		CH22_FGENES.140_3	1.1
313150	EOS13081	AA824410	Hs.165003	ESTs	1.1
339208	EOS39139	CH22_8146FG__LINK_FF113D11.GENSCAN.6-3		CH22_FF113D11.GENSCAN.6-3	1.1
335653	EOS35584	CH22_3013FG_590_4_LINK_EM:AC005500.GENSCAN.484-4		CH22_FGENES.590_4	1.1
319524	EOS19455	AA682865	Hs.194441	ESTs	1.1
301576	EOS01507	AI682905	Hs.146875	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.1
317598	EOS17529	AW206035	Hs.192123	ESTs	1.1
333473	EOS33404	CH22_724FG_162_3_LINK_EM:AC005500.GENSCAN.42-10		CH22_FGENES.162_3	1.1
333949	EOS33880	CH22_1225FG_303_5_LINK_EM:AC005500.GENSCAN.162-9		CH22_FGENES.303_5	1.1
339256	EOS39187	CH22_8207FG__LINK_BA354I12.GENSCAN.7-11		CH22_BA354I12.GENSCAN.7-11	1.1
332884	EOS32815	CH22_104FG_33_5_LINK_C20H12.GENSCAN.22-7		CH22_FGENES.33_5	1.1
314660	EOS14591	AA436007	Hs.188780	ESTs	1.1
333220	EOS33151	CH22_457FG_104_12_LINK_EM:AC000097.GENSCAN.108-11		CH22_FGENES.104_12	1.1
308106	EOS08037	AI476803		EST singleton (not in UniGene) with exon hit	1.1
320709	EOS20640	AA456660	Hs.154165	ESTs	1.1
307612	EOS07543	AI290787		EST singleton (not in UniGene) with exon hit	1.1
330286	EOS30217	c_5_p2 gi|6671913|gb|A gn 2 - 31050 31171 ex 2 7 CDSl 8.84 122 791		CH.05_p2 gi|6671913	1.1
304495	EOS04426	AA446448		EST singleton (not in UniGene) with exon hit	1.1
310583	EOS10514	AW205632	Hs.211198	ESTs	1.1
332896	EOS32827	CH22_117FG_35_10_LINK_C20H12.GENSCAN.24-9		CH22_FGENES.35_10	1.1
337602	EOS37533	CH22_5895FG__LINK_C20H12.GENSCAN.15-1		CH22_C20H12.GENSCAN.15-1	1.1
307626	EOS07557	AI300035		EST singleton (not in UniGene) with exon hit	1.1
334696	EOS34627	CH22_2006FG_421_5_LINK_EM:AC005500.GENSCAN.282-5		CH22_FGENES.421_5	1.1
318652	EOS18583	T53259		EST cluster (not in UniGene)	1.1
337844	EOS37775	CH22_6229FG__LINK_EM:AC005500.GENSCAN.30-9		CH22_EM:AC005500.GENSCAN.30-9	1.1
334823	EOS34754	CH22_2137FG_437_5_LINK_EM:AC005500.GENSCAN.301-7		CH22_FGENES.437_5	1.1
333928	EOS33859	CH22_1201FG_299_2_LINK_EM:AC005500.GENSCAN.158-5		CH22_FGENES.299_2	1.1
337503	EOS37434	CH22_5738FG_803_1_		CH22_FGENES.803-1	1.1
323044	EOS22975	AA148725	Hs.154190	ESTs	1.1
329164	EOS29095	c_x_hs gi|5868691|ref| gn 1 + 62305 62517 ex 2 2 CDSl 17.51 213 1868		CH.X_hs gi|5868691	1.1
335468	EOS35399	CH22_2819FG_567_4_LINK_EM:AC005500.GENSCAN.454-12		CH22_FGENES.567_4	1.1
338962	EOS38893	CH22_7838FG__LINK_DJ32I10.GENSCAN.23-39		CH22_DJ32I10.GENSCAN.23-39	1.1
323570	EOS23501	AL038623	Hs.208752	ESTs; Weakly similar to !!!! ALU SUBFAMILY SX WARNING ENTRY !!!! [H.sapiens]	1.1
333568	EOS33499	CH22_826FG_185_1_LINK_EM:AC005500.GENSCAN.64-1		CH22_FGENES.185_1	1.1
331865	EOS31796	AA425756	Hs.98445	ESTs	1.1
336246	EOS36177	CH22_3644FG_746_5_LINK_DA59H18.GENSCAN.48-4		CH22_FGENES.746_5	1.1
337238	EOS37169	CH22_5343FG_641_3_		CH22_FGENES.641-3	1.1

305089	EOS05020	AA642622		EST singleton (not in UniGene) with exon hit	1.1
300097	EOS00028	AI916973	Hs.213603	ESTs	1.1
313134	EOS13065	N63406	Hs.258697	ESTs	1.1
337452	EOS37383	CH22_5665FG_775_1_		CH22_FGENES.775-1	1.1
325433	EOS25364	c12_hs gi|5866936|ref| gn 4 - 480706 480826 ex 3 4 CDSI 1.99 121 818		CH.12_hs gi|5866936	1.1
335999	EOS35930	CH22_3380FG_657_1_LINK_DJ246D7.GENSCAN.11-1		CH22_FGENES.657_1	1.1
333580	EOS33511	CH22_840FG_199_2_LINK_EM:AC005500.GENSCAN.71-2		CH22_FGENES.199_2	1.1
336836	EOS36767	CH22_4512FG_247_11_		CH22_FGENES.247-11	1.1
334677	EOS34608	CH22_1986FG_418_30_LINK_EM:AC005500.GENSCAN.279-31		CH22_FGENES.418_30	1.1
329062	EOS28993	c_x_hs gi|5868590|ref| gn 3 - 58977 59094 ex 4 11 CDSI -6.19 118 627		CH.X_hs gi|5868590	1.1
333671	EOS33602	CH22_932FG_245_5_LINK_EM:AC005500.GENSCAN.100-12		CH22_FGENES.245_5	1.1
304941	EOS04872	AA612612		EST singleton (not in UniGene) with exon hit	1.1
315772	EOS15703	AW515373	Hs.158893	ESTs	1.1
301281	EOS01212	AA843986	Hs.190586	ESTs	1.1
333520	EOS33451	CH22_777FG_174_3_LINK_EM:AC005500.GENSCAN.53-6		CH22_FGENES.174_3	1.1
315203	EOS15134	AI559820	Hs.199438	ESTs	1.1
315927	EOS15858	AW025517	Hs.133250	ESTs	1.1
317161	EOS17092	AA972165	Hs.150308	ESTs	1.1
337692	EOS37623	CH22_6028FG__LINK_EM:AC000097.GENSCAN.78-12		CH22_EM:AC000097.GENSCAN.78-12	1.1
331472	EOS31403	N24830		yx70a02.s1 Soares melanocyte 2NbHM Homo sapiens cDNA clone IMAGE:267050 3' similar to gb|M87912|HUMALNE562 Human carcinoma cell-derived Alu RNA transcript, (rRNA);contains Alu repetitive element;, mRNA sequence.	1.1
336439	EOS36370	CH22_3859FG_827_4_LINK_DJ579N16.GENSCAN.1-3		CH22_FGENES.827_4	1.1
326882	EOS26813	c20_hs gi|6682509|ref| gn 2 - 167988 168179 ex 4 4 CDSf 18.69 192 2238		CH.20_hs gi|6682509	1.1
336977	EOS36908	CH22_4793FG_380_9_		CH22_FGENES.380-9	1.1
333983	EOS33914	CH22_1260FG_310_7_LINK_EM:AC005500.GENSCAN.167-5		CH22_FGENES.310_7	1.1
328878	EOS28809	c_7_hs gi|6552423|ref| gn 1 + 105580 105774 ex 6 7 CDSI 2.91 195 6195		CH.07_hs gi|6552423	1.1
330415	EOS30346	D83777	Hs.75137	KIAA0193 gene product	1.1
324824	EOS24755	AI826999	Hs.224624	ESTs	1.1
325815	EOS25746	c14_hs gi|6682483|ref| gn 1 - 129273 130754 ex 1 1 CDSo 11.82 1482 2225		CH.14_hs gi|6682483	1.1
300463	EOS00394	N52510	Hs.186470	ESTs	1.1
335708	EOS35639	CH22_3069FG_599_8_LINK_EM:AC005500.GENSCAN.490-11		CH22_FGENES.599_8	1.1
324575	EOS24506	AW502257		EST cluster (not in UniGene)	1.1
337951	EOS37882	CH22_6391FG__LINK_EM:AC005500.GENSCAN.94-1		CH22_EM:AC005500.GENSCAN.94-1	1.1
335935	EOS35866	CH22_3313FG_646_6_LINK_DJ246D7.GENSCAN.1-5		CH22_FGENES.646_6	1.1
334914	EOS34845	CH22_2233FG_457_3_LINK_EM:AC005500.GENSCAN.346-2		CH22_FGENES.457_3	1.1
309527	EOS09458	AW150648	Hs.75621	protease inhibitor 1 (anti-elastase); alpha-1-antitrypsin	1.1
318901	EOS18832	AW368520	Hs.24639	ESTs	1.1
320484	EOS20415	AA094436	Hs.155712	follistatin-like 1	1.1
333665	EOS33596	CH22_926FG_244_1_LINK_EM:AC005500.GENSCAN.99-1		CH22_FGENES.244_1	1.1
335860	EOS35791	CH22_3235FG_629_5_LINK_EM:AC005500.GENSCAN.519-4		CH22_FGENES.629_5	1.1
313339	EOS13270	AI682536	Hs.163495	ESTs	1.1
300149	EOS00080	AW448916	Hs.149018	ESTs	1.1
318112	EOS18043	AI028162	Hs.132307	ESTs	1.1
337807	EOS37738	CH22_6178FG__LINK_EM:AC005500.GENSCAN.9-4		CH22_EM:AC005500.GENSCAN.9-4	1.1
336917	EOS36848	CH22_4688FG_346_4_		CH22_FGENES.346-4	1.1
337489	EOS37420	CH22_5722FG_799_2_		CH22_FGENES.799-2	1.1
320112	EOS20043	T92107	Hs.188489	ESTs	1.1
332975	EOS32906	CH22_199FG_51_10_LINK_EM:AC000097.GENSCAN.4-12		CH22_FGENES.51_10	1.1
327805	EOS27736	c_5_hs gi|5867968|ref| gn 2 + 19952 20019 ex 1 2 CDSf 9.47 68 988		CH.05_hs gi|5867968	1.1
339215	EOS39146	CH22_8153FG__LINK_FF113D11.GENSCAN.6-10		CH22_FF113D11.GENSCAN.6-10	1.1
311965	EOS11896	T69279		EST cluster (not in UniGene)	1.1
314043	EOS13974	AA827082		EST cluster (not in UniGene)	1.1
333447	EOS33378	CH22_697FG_154_5_LINK_EM:AC005500.GENSCAN.35-6		CH22_FGENES.154_5	1.1
333242	EOS33173	CH22_481FG_111_6_LINK_EM:AC000097.GENSCAN.120-5		CH22_FGENES.111_6	1.1
338596	EOS38527	CH22_7343FG__LINK_EM:AC005500.GENSCAN.437-2		CH22_EM:AC005500.GENSCAN.437-2	1.1
329989	EOS29920	c16_p2 gi|4567166|gb|A gn 2 + 72861 73052 ex 1 3 CDSf 18.02 192 590		CH.16_p2 gi|4567166	1.1
315675	EOS15606	AA652272	Hs.197320	ESTs	1.1
336722	EOS36653	CH22_4245FG_84_2_		CH22_FGENES.84-2	1.1

334220	EOS34151	CH22_1503FG_359_4_LINK_EM:AC005500.GENSCAN.217-7			
				CH22_FGENES.359_4	1.1
336703	EOS36634	CH22_4201FG_56_3_		CH22_FGENES.56-3	1.1
336397	EOS36328	CH22_3812FG_823_12_LINK_BA232E17.GENSCAN.6-11			
				CH22_FGENES.823_12	1.1
316105	EOS16036	AW295687	Hs.254420	ESTs	1.1
334661	EOS34592	CH22_1969FG_418_9_LINK_EM:AC005500.GENSCAN.279-13			
				CH22_FGENES.418_9	1.1
307783	EOS07714	AI347274		EST singleton (not in UniGene) with exon hit	1.1
333997	EOS33928	CH22_1275FG_310_22_LINK_EM:AC005500.GENSCAN.167-21			
				CH22_FGENES.310_22	1.1
331903	EOS31834	AA436673	Hs.29417	Homo sapiens mRNA; cDNA DKFZp586B0323 (from clone DKFZp586B0323)	1.1
328249	EOS28180	c_6_hs gi|6381891|ref| gn 2 - 96352 96527 ex 2 3 CDSI 6.19 176 4550			
				CH.06_hs gi|6381891	1.1
338251	EOS38182	CH22_6849FG__LINK_EM:AC005500.GENSCAN.270-1			
				CH22_EM:AC005500.GENSCAN.270-1	1.1
323561	EOS23492	AA825426	Hs.238832	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.1
301464	EOS01395	AA991519	Hs.253324	ESTs	1.1
335916	EOS35847	CH22_3293FG_636_12_LINK_EM:AC005500.GENSCAN.526-12			
				CH22_FGENES.636_12	1.1
321828	EOS21759	X56197		EST cluster (not in UniGene)	1.1
327413	EOS27344	c_2_hs gi|5867750|ref| gn 3 + 101410 101508 ex 4 5 CDSI 4.34 99 587			
				CH.02_hs gi|5867750	1.1
334474	EOS34405	CH22_1773FG_394_5_LINK_EM:AC005500.GENSCAN.257-5			
				CH22_FGENES.394_5	1.1
336739	EOS36670	CH22_4291FG_117_3_		CH22_FGENES.117-3	1.1
316517	EOS16448	AI784315	Hs.123163	ESTs	1.1
325519	EOS25450	c12_hs gi|6017036|ref| gn 5 - 186804 186915 ex 1 3 CDSI 8.36 112 2508			
				CH.12_hs gi|6017036	1.1
333875	EOS33806	CH22_1145FG_291_11_LINK_EM:AC005500.GENSCAN.149-6			
				CH22_FGENES.291_11	1.1
338221	EOS38152	CH22_6797FG__LINK_EM:AC005500.GENSCAN.246-10			
				CH22_EM:AC005500.GENSCAN.246-10	1.1
336878	EOS36809	CH22_4617FG_318_5_		CH22_FGENES.318-5	1.1
337919	EOS37850	CH22_6338FG__LINK_EM:AC005500.GENSCAN.66-5			
				CH22_EM:AC005500.GENSCAN.66-5	1.1
309828	EOS09759	AW293999		EST singleton (not in UniGene) with exon hit	1.1
305259	EOS05190	AA679225		EST singleton (not in UniGene) with exon hit	1.1
333922	EOS33853	CH22_1195FG_296_13_LINK_EM:AC005500.GENSCAN.155-16			
				CH22_FGENES.296_13	1.1
322092	EOS22023	AF085833		EST cluster (not in UniGene)	1.1
313356	EOS13287	AI266254	Hs.132929	ESTs	1.1
318847	EOS18778	Z42908	Hs.12308	ESTs	1.1
337175	EOS37106	CH22_5195FG_567_1_		CH22_FGENES.567-1	1.1
336979	EOS36910	CH22_4802FG_385_4_		CH22_FGENES.385-4	1.1
312169	EOS12100	AI064824	Hs.193385	ESTs	1.1
336198	EOS36129	CH22_3595FG_719_2_LINK_DA59H18.GENSCAN.21-2			
				CH22_FGENES.719_2	1.1
321948	EOS21879	AA309612	Hs.118797	ubiquitin-conjugating enzyme E2D 3 (homologous to yeast UBC4/5)	1.1
324692	EOS24623	AA557952		EST cluster (not in UniGene)	1.1
330395	EOS30326	D10923	Hs.137555	putative chemokine receptor; GTP-binding protein	1.1
333119	EOS33050	CH22_347FG_80_4_LINK_EM:AC000097.GENSCAN.65-4			
				CH22_FGENES.80_4	1.1
316012	EOS15943	AA764950	Hs.119898	ESTs	1.1
300142	EOS00073	AI743419	Hs.205707	ESTs	1.1
317215	EOS17146	AW014242	Hs.159998	ESTs	1.1
329526	EOS29457	c10_p2 gi|3983506|gb|U gn 2 + 12251 12325 ex 3 3 CDSI 7.37 75 178			
				CH.10_p2 gi|3983506	1.1
317409	EOS17340	AA764968	Hs.4864	KIAA0892 protein	1.1
339230	EOS39161	CH22_8171FG__LINK_BA354I12.GENSCAN.1-6			
				CH22_BA354I12.GENSCAN.1-6	1.1
311598	EOS11529	AW023595	Hs.232048	ESTs	1.1
339164	EOS39095	CH22_8091FG__LINK_DA59H18.GENSCAN.69-4			
				CH22_DA59H18.GENSCAN.69-4	1.1
326725	EOS26656	c20_hs gi|6552456|ref| gn 2 - 223005 223125 ex 5 6 CDSI 6.10 121 1038			
				CH.20_hs gi|6552456	1.1
330952	EOS30883	H02855	Hs.29567	ESTs	1.1
334621	EOS34552	CH22_1928FG_412_4_LINK_EM:AC005500.GENSCAN.275-4			
				CH22_FGENES.412_4	1.1
301685	EOS01616	W67730		EST cluster (not in UniGene) with exon hit	1.1
308781	EOS08712	AI811707		EST singleton (not in UniGene) with exon hit	1.1
323413	EOS23344	AA248828	Hs.225676	ESTs	1.1
306723	EOS06654	AI026151		EST singleton (not in UniGene) with exon hit	1.1
331258	EOS31189	Z41777	Hs.27413	ESTs	1.1
313028	EOS12959	AI355433	Hs.190856	ESTs	1.1
333002	EOS32933	CH22_226FG_59_3_LINK_EM:AC000097.GENSCAN.21-3			
				CH22_FGENES.59_3	1.1
303011	EOS02942	AF090405		EST cluster (not in UniGene) with exon hit	1.1
317687	EOS17618	AA972990	Hs.127904	ESTs	1.1
328779	EOS28710	c_7_hs gi|5868309|ref| gn 4 + 41570 41639 ex 1 5 CDSf 2.65 70 5365			
				CH.07_hs gi|5868309	1.1
338707	EOS38638	CH22_7487FG__LINK_EM:AC005500.GENSCAN.482-2			
				CH22_EM:AC005500.GENSCAN.482-2	1.1
337974	EOS37905	CH22_6427FG__LINK_EM:AC005500.GENSCAN.106-3			
				CH22_EM:AC005500.GENSCAN.106-3	1.1
332854	EOS32785	CH22_71FG_22_1_LINK_C20H12.GENSCAN.15-2			

				CH22_FGENES.22_1	1.1
311225	EOS11156	AW451982	Hs.248613	ESTs	1.1
337094	EOS37025	CH22_5018FG_465_19_		CH22_FGENES.465-19	1.1
319357	EOS19288	F13425	Hs.26229	ESTs	1.1
332958	EOS32889	CH22_182FG_48_15_LINK_EM:AC000097.GENSCAN.2-11		CH22_FGENES.48_15	1.1
309634	EOS09565	AW193825		EST singleton (not in UniGene) with exon hit	1.1
321171	EOS21102	AI769410	Hs.221461	ESTs	1.1
316440	EOS16371	AI954795	Hs.156135	ESTs	1.1
311665	EOS11596	AW294254	Hs.223742	ESTs	1.1
327548	EOS27479	c_3_hs gi|5867797|ref| gn 2 - 81067 81130 ex 3 7 CDSI 6.42 64 12		CH.03_hs gi|5867797	1.1
314940	EOS14871	AW452768	Hs.162045	ESTs	1.1
326401	EOS26332	c19_hs gi|5867355|ref| gn 1 + 35165 35332 ex 9 11 CDSI 0.41 168 788		CH.19_hs gi|5867355	1.1
336347	EOS36278	CH22_3759FG_815_3_LINK_BA232E17.GENSCAN.1-24		CH22_FGENES.815_3	1.1
322297	EOS22228	W76548	Hs.136026	ESTs; Moderately similar to !!!! ALU SUBFAMILY SC WARNING ENTRY !!!! [H.sapiens]	1.1
309977	EOS09908	AW451663		EST singleton (not in UniGene) with exon hit	1.1
333466	EOS33397	CH22_717FG_161_2_LINK_EM:AC005500.GENSCAN.42-2		CH22_FGENES.161_2	1.1
329170	EOS29101	c_x_hs gi|5868693|ref| gn 2 + 67924 68019 ex 6 8 CDSI 3.30 96 1882		CH.X_hs gi|5868693	1.1
329479	EOS29410	c10_p2 gi|3983526|gb|A gn 3 - 7425 7561 ex 1 3 CDSI 4.33 137 22		CH.10_p2 gi|3983526	1.1
326668	EOS26599	c20_hs gi|6552455|ref| gn 1 + 146726 146838 ex 11 11 CDSI 1.84 113 767		CH.20_hs gi|6552455	1.1
319364	EOS19295	H06538	Hs.12270	ESTs	1.1
302988	EOS02919	W23986	Hs.34578	alpha2;3-sialyltransferase	1.1
327687	EOS27618	c_4_hs gi|5867847|ref| gn 1 - 169293 169362 ex 2 3 CDSI -0.28 70 782		CH.04_hs gi|5867847	1.1
339413	EOS39344	CH22_8405FG__LINK_DJ579N16.GENSCAN.5-8		CH22_DJ579N16.GENSCAN.5-8	1.1
306156	EOS06087	AA918274	Hs.76067	heat shock 27kD protein 1	1.1
320858	EOS20789	D59968		EST cluster (not in UniGene)	1.1
325447	EOS25378	c12_hs gi|5866941|ref| gn 3 - 372480 372621 ex 2 3 CDSI 9.16 142 1026		CH.12_hs gi|5866941	1.1
322696	EOS22627	AI064724	Hs.228468	ESTs	1.1
329959	EOS29890	c16_p2 gi|5103803|gb|A gn 3 + 188050 188193 ex 8 8 CDSI 2.01 144 361		CH.16_p2 gi|5103803	1.1
312628	EOS12559	AA632817	Hs.190316	ESTs	1.1
339305	EOS39236	CH22_8262FG__LINK_BA354I12.GENSCAN.21-3		CH22_BA354I12.GENSCAN.21-3	1.1
311829	EOS11760	AI078483	Hs.134549	ESTs	1.1
303270	EOS03201	AL120518	Hs.105352	ESTs	1.1
321226	EOS21157	AA311443	Hs.251416	Homo sapiens mRNA; cDNA DKFZp586E2317 (from clone DKFZp586E2317)	1.1
335827	EOS35758	CH22_3200FG_620_1_LINK_EM:AC005500.GENSCAN.512-1		CH22_FGENES.620_1	1.1
336677	EOS36608	CH22_4155FG_43_5_		CH22_FGENES.43-5	1.1
330081	EOS30012	c19_p2 gi|6015314|gb|A gn 1 - 5768 5835 ex 4 9 CDSI 2.88 68 162		CH.19_p2 gi|6015314	1.1
339313	EOS39244	CH22_8272FG__LINK_BA354I12.GENSCAN.22-11		CH22_BA354I12.GENSCAN.22-11	1.1
319936	EOS19867	W22152		EST cluster (not in UniGene)	1.1
332858	EOS32789	CH22_76FG_24_1_LINK_C20H12.GENSCAN.16-6		CH22_FGENES.24_1	1.1
315630	EOS15561	AA648355	Hs.185155	ESTs; Weakly similar to echinoderm microtubule-associated protein-like EMAP2 [H.sapiens]	1.1
332995	EOS32926	CH22_219FG_58_2_LINK_EM:AC000097.GENSCAN.19-2		CH22_FGENES.58_2	1.1
333441	EOS33372	CH22_691FG_151_5_LINK_EM:AC005500.GENSCAN.32-5		CH22_FGENES.151_5	1.1
333496	EOS33427	CH22_748FG_168_6_LINK_EM:AC005500.GENSCAN.47-5		CH22_FGENES.168_6	1.1
339188	EOS39119	CH22_8123FG__LINK_DA59H18.GENSCAN.72-16		CH22_DA59H18.GENSCAN.72-16	1.1
336981	EOS36912	CH22_4818FG_397_7_		CH22_FGENES.397-7	1.1
312142	EOS12073	AW298359	Hs.221069	ESTs	1.1
315779	EOS15710	AW015736	Hs.211378	ESTs	1.1
318596	EOS18527	AI470235	Hs.172698	EST	1.1
335701	EOS35632	CH22_3062FG_599_1_LINK_EM:AC005500.GENSCAN.490-2		CH22_FGENES.599_1	1.1
319395	EOS19326	AW062570	Hs.13809	ESTs	1.1
304236	EOS04167	W93278		EST singleton (not in UniGene) with exon hit	1.1
307264	EOS07195	AI202211		EST singleton (not in UniGene) with exon hit	1.1
334066	EOS33997	CH22_1344FG_327_21_LINK_EM:AC005500.GENSCAN.181-23		CH22_FGENES.327_21	1.1
327042	EOS26973	c21_hs gi|6531965|ref| gn 18 - 1380806 1381443 ex 1 5 CDSI 30.85 638 943		CH.21_hs gi|6531965	1.1
326025	EOS25956	c17_hs gi|5867176|ref| gn 1 + 70854 70915 ex 6 8 CDSI -1.46 62 127		CH.17_hs gi|5867176	1.1
325609	EOS25540	c14_hs gi|5866996|ref| gn 28 - 981751 981849 ex 1 10 CDSI 1.46 99 101		CH.14_hs gi|5866996	1.1
319983	EOS19914	T81429		EST cluster (not in UniGene)	1.1
334298	EOS34229	CH22_1589FG_372_4_LINK_EM:AC005500.GENSCAN.232-5		CH22_FGENES.372_4	1.1
323203	EOS23134	AA203135	Hs.130186	ESTs	1.1

305700	EOS05631	AA815428		EST singleton (not in UniGene) with exon hit	1.1
313304	EOS13235	AI334078	Hs.152438	ESTs	1.1
310716	EOS10647	AI589618	Hs.192413	ESTs	1.1
327049	EOS26980	c21_hs gi|6531965|ref| gn 24 - 1924026 1924110 ex 2 6 CDSi 9.43 85 1012		CH.21_hs gi|6531965	1.1
313749	EOS13680	AW450376	Hs.130803	ESTs	1.1
307041	EOS06972	AI144243		EST singleton (not in UniGene) with exon hit	1.1
322394	EOS22325	AF077208		EST cluster (not in UniGene)	1.1
326416	EOS26347	c19_hs gi|5867362|ref| gn 3 - 45283 45375 ex 3 3 CDSf 5.65 93 923		CH.19_hs gi|5867362	1.1
333947	EOS33878	CH22_1221FG_303_1_LINK_EM:AC005500.GENSCAN.162-5		CH22_FGENES.303_1	1.1
324609	EOS24540	AW299534		EST cluster (not in UniGene)	1.1
330057	EOS29988	c17_p2 gi|6478962|gb|A gn 3 + 75145 75287 ex 3 3 CDSI -2.56 143 150		CH.17_p2 gi|6478962	1.1
337603	EOS37534	CH22_5896FG__LINK_C20H12.GENSCAN.16-2		CH22_C20H12.GENSCAN.16-2	1.1
332913	EOS32844	CH22_134FG_36_18_LINK_C20H12.GENSCAN.28-17		CH22_FGENES.36_18	1.1
310026	EOS09957	T24895	Hs.100691	ESTs	1.1
330153	EOS30084	c21_p2 gi|4325335|gb|A gn 2 + 146951 147475 ex 2 2 CDSI 25.45 525 233		CH.21_p2 gi|4325335	1.1
334118	EOS34049	CH22_1396FG_330_19_LINK_EM:AC005500.GENSCAN.185-20		CH22_FGENES.330_19	1.1
324795	EOS24726	AI494481	Hs.141579	ESTs	1.1
332530	EOS32461	M31682	Hs.1735	inhibin; beta B (activin AB beta polypeptide)	1.1
332048	EOS31979	AA496019	Hs.201591	ESTs	1.1
334532	EOS34463	CH22_1834FG_402_13_LINK_EM:AC005500.GENSCAN.266-13		CH22_FGENES.402_13	1.1
329762	EOS29693	c14_p2 gi|6048280|emb| gn 3 + 127744 127878 ex 2 4 CDSI 11.66 135 1054		CH.14_p2 gi|6048280	1.1
332909	EOS32840	CH22_130FG_36_13_LINK_C20H12.GENSCAN.28-10		CH22_FGENES.36_13	1.1
321253	EOS21184	AI699484		EST cluster (not in UniGene)	1.1
336572	EOS36503	CH22_4007FG_843_12_LINK_DJ579N16.GENSCAN.15-13		CH22_FGENES.843_12	1.1
328768	EOS28699	c_7_hs gi|6017031|ref| gn 5 - 223741 224238 ex 1 1 CDSo 30.00 498 5285		CH.07_hs gi|6017031	1.1
334335	EOS34266	CH22_1627FG_375_12_LINK_EM:AC005500.GENSCAN.235-12		CH22_FGENES.375_12	1.1
334063	EOS33994	CH22_1341FG_327_17_LINK_EM:AC005500.GENSCAN.181-20		CH22_FGENES.327_17	1.1
333011	EOS32942	CH22_235FG_61_3_LINK_EM:AC000097.GENSCAN.23-3		CH22_FGENES.61_3	1.1
304677	EOS04608	AA548071		EST singleton (not in UniGene) with exon hit	1.1
313948	EOS13879	AW452823	Hs.135268	ESTs	1.1
334358	EOS34289	CH22_1652FG_378_1_LINK_EM:AC005500.GENSCAN.239-1		CH22_FGENES.378_1	1.1
328479	EOS28410	c_7_hs gi|5868449|ref| gn 1 - 331 560 ex 1 31 CDSI 18.51 230 2100		CH.07_hs gi|5868449	1.1
335813	EOS35744	CH22_3185FG_618_1_LINK_EM:AC005500.GENSCAN.510-1		CH22_FGENES.618_1	1.1
312430	EOS12361	AW139117	Hs.117494	ESTs	1.1
324783	EOS24714	AA640770		EST cluster (not in UniGene)	1.1
337776	EOS37707	CH22_6132FG__LINK_EM:AC000097.GENSCAN.119-18		CH22_EM:AC000097.GENSCAN.119-18	1.1
327205	EOS27136	c_1_hs gi|5867447|ref| gn 5 + 167335 167576 ex 9 9 CDSI 15.50 242 259		CH.01_hs gi|5867447	1.1
315198	EOS15129	AI741506	Hs.186753	ESTs; Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.1
336135	EOS36066	CH22_3525FG_704_3_LINK_DA59H18.GENSCAN.9-5		CH22_FGENES.704_3	1.1
318558	EOS18489	AW402677	Hs.90372	ESTs	1.1
328152	EOS28083	c_6_hs gi|5868060|ref| gn 1 - 73981 74203 ex 1 8 CDSI 31.69 223 3411		CH.06_hs gi|5868060	1.1
330211	EOS30142	c_5_p2 gi|6013592|gb|A gn 1 + 59158 59215 ex 2 4 CDSI 4.20 58 184		CH.05_p2 gi|6013592	1.1
339280	EOS39211	CH22_8234FG__LINK_BA354I12.GENSCAN.14-12		CH22_BA354I12.GENSCAN.14-12	1.1
332045	EOS31976	AA491253	Hs.155045	bromodomain adjacent to zinc finger domain; 2A	1.1
313597	EOS13528	AW162263	Hs.249990	ESTs	1.1
329503	EOS29434	c10_p2 gi|3983517|gb|U gn 2 - 1801 1937 ex 1 4 CDSI 4.33 137 101		CH.10_p2 gi|3983517	1.1
333488	EOS33419	CH22_740FG_167_3_LINK_EM:AC005500.GENSCAN.46-10		CH22_FGENES.167_3	1.1
311960	EOS11891	AW440133	Hs.189690	ESTs	1.1
320590	EOS20521	U67058	Hs.168102	Human proteinase activated receptor-2 mRNA; 3'UTR	1.1
334047	EOS33978	CH22_1325FG_326_5_LINK_EM:AC005500.GENSCAN.175-5		CH22_FGENES.326_5	1.1
304782	EOS04713	AA582081		EST singleton (not in UniGene) with exon hit	1.1
324231	EOS24162	W60827		EST cluster (not in UniGene)	1.1
327212	EOS27143	c_1_hs gi|5867463|ref| gn 1 - 42308 42424 ex 5 13 CDSI 6.58 117 325		CH.01_hs gi|5867463	1.1
335857	EOS35788	CH22_3232FG_629_1_LINK_EM:AC005500.GENSCAN.519-1		CH22_FGENES.629_1	1.1
317775	EOS17706	AA974603	Hs.181123	ESTs	1.1
331053	EOS30984	N70242	Hs.183146	ESTs	1.1

335940	EOS35871	CH22_3318FG_646_13_LINK_DJ246D7.GENSCAN.1-12		CH22_FGENES.646_13	1.1
322568	EOS22499	W87342	Hs.209652	ESTs	1.1
314091	EOS14022	AI253112	Hs.133540	ESTs	1.1
313570	EOS13501	AA041455	Hs.209312	ESTs	1.1
300967	EOS00898	AA565209	Hs.190216	ESTs	1.1
314544	EOS14475	AA399018	Hs.250835	ESTs	1.1
328321	EOS28252	c_7_hs gi|5868373|ref| gn 7 - 1029614 1029673 ex 1 3 CDSI -2.40 60 448		CH.07_hs gi|5868373	1.1
310979	EOS10910	AW445166	Hs.170802	ESTs	1.1
310730	EOS10661	AI939421	Hs.160900	ESTs	1.1
318471	EOS18402	AW137725	Hs.146874	ESTs	1.1
315533	EOS15464	AW206191	Hs.152774	ESTs	1.1
325751	EOS25682	c14_hs gi|6682474|ref| gn 4 + 130437 130520 ex 6 7 CDSI 0.22 84 1666		CH.14_hs gi|6682474	1.1
318780	EOS18711	R90906	Hs.113307	ESTs	1.1
313271	EOS13202	AW444819	Hs.144851	ESTs; Weakly similar to C09F5.2 [C.elegans]	1.1
304546	EOS04477	AA486074		EST singleton (not in UniGene) with exon hit	1.1
330618	EOS30549	X55990	Hs.73839	ribonuclease; RNase A family; 3 (eosinophil cationic protein)	1.1
332931	EOS32862	CH22_152FG_38_5_LINK_C20H12.GENSCAN.29-5		CH22_FGENES.38_5	1.1
336602	EOS36533	CH22_4047FG_372_4_LINK_EM:AC005500.GENSCAN.232-4		CH22_FGENES.372_4	1.1
311185	EOS11116	AI638294	Hs.224665	ESTs	1.1
337585	EOS37516	CH22_5873FG__LINK_C20H12.GENSCAN.5-3		CH22_C20H12.GENSCAN.5-3	1.1
310249	EOS10180	AW071751	Hs.13179	ESTs; Moderately similar to !!!! ALU SUBFAMILY SQ WARNING ENTRY !!!! [H.sapiens]	1.1
314578	EOS14509	AA410183	Hs.137475	ESTs	1.1
310750	EOS10681	AI373163	Hs.170333	ESTs	1.1
333968	EOS33899	CH22_1245FG_307_4_LINK_EM:AC005500.GENSCAN.165-5		CH22_FGENES.307_4	1.1
316133	EOS16064	AI187742	Hs.125562	ESTs	1.1
308337	EOS08268	AI608947		EST singleton (not in UniGene) with exon hit	1.1
326160	EOS26091	c17_hs gi|5867254|ref| gn 6 - 112000 112137 ex 2 4 CDSi 8.01 138 1952		CH.17_hs gi|5867254	1.1
336023	EOS35954	CH22_3406FG_669_12_LINK_DJ32I10.GENSCAN.9-17		CH22_FGENES.669_12	1.1
323479	EOS23410	AA278246		EST cluster (not in UniGene)	1.1
336090	EOS36021	CH22_3477FG_689_2_LINK_DJ32I10.GENSCAN.23-20		CH22_FGENES.689_2	1.1
311192	EOS11123	AW237220	Hs.211130	ESTs	1.1
335081	EOS35012	CH22_2409FG_488_4_LINK_EM:AC005500.GENSCAN.384-6		CH22_FGENES.488_4	1.1
309519	EOS09450	AW148940	Hs.248647	EST	1.1
321172	EOS21103	H49160	Hs.133472	ESTs	1.1
301976	EOS01907	T97905		EST cluster (not in UniGene) with exon hit	1.1
323012	EOS22943	AI832201	Hs.211469	ESTs	1.1
319528	EOS19459	R08673	Hs.177514	ESTs	1.1
329838	EOS29769	c14_p2 gi|6672062|emb| gn 2 + 33990 34098 ex 3 4 CDSI 9.11 109 2222		CH.14_p2 gi|6672062	1.1
302623	EOS02554	AB019571		EST cluster (not in UniGene) with exon hit	1.1
334433	EOS34364	CH22_1731FG_385_8_LINK_EM:AC005500.GENSCAN.249-6		CH22_FGENES.385_8	1.1
304747	EOS04678	AA577816		EST singleton (not in UniGene) with exon hit	1.1
333270	EOS33201	CH22_513FG_121_1_LINK_EM:AC005500.GENSCAN.4-11		CH22_FGENES.121_1	1.1
307054	EOS06985	AI148181	Hs.176835	EST	1.1
320764	EOS20695	R73070	Hs.246927	ESTs	1.1
321523	EOS21454	H78472	Hs.191325	ESTs; Weakly similar to cDNA EST yk414c9.3 comes from this gene [C.elegans]	1.1
322114	EOS22045	AA643791	Hs.191740	ESTs	1.1
303582	EOS03513	AA377444		EST cluster (not in UniGene) with exon hit	1.1
322924	EOS22855	AA669253	Hs.193971	ESTs	1.1
311179	EOS11110	AI880843	Hs.223333	ESTs	1.1
318601	EOS18532	T39921		EST cluster (not in UniGene)	1.1
309791	EOS09722	AW276176	Hs.73742	ribosomal protein; large; P0	1.1
333882	EOS33813	CH22_1153FG_292_4_LINK_EM:AC005500.GENSCAN.150-4		CH22_FGENES.292_4	1.1
337645	EOS37576	CH22_5960FG__LINK_EM:AC000097.GENSCAN.10-8		CH22_EM:AC000097.GENSCAN.10-8	1.1
335623	EOS35554	CH22_2983FG_584_2_LINK_EM:AC005500.GENSCAN.478-2		CH22_FGENES.584_2	1.1
314745	EOS14676	AA564489	Hs.137526	ESTs	1.1
330790	EOS30721	T48536	Hs.105807	ESTs	1.1
332071	EOS32002	AA598594	Hs.112475	ESTs	1.1
312005	EOS11936	T78450	Hs.13941	ESTs	1.1
330694	EOS30625	AA019806	Hs.108447	spinocerebellar ataxia 7 (olivopontocerebellar atrophy with retinal degeneration)	1.1
330739	EOS30670	AA293477	Hs.227591	ESTs	1.1
303042	EOS02973	AF129532		EST cluster (not in UniGene) with exon hit	1.1
323091	EOS23022	AW014094	Hs.210761	ESTs	1.1
328820	EOS28751	c_7_hs gi|5868330|ref| gn 1 + 90446 90602 ex 3 4 CDSI 10.20 157 5634		CH.07_hs gi|5868330	1.1
300472	EOS00403	T90622	Hs.82609	hydroxymethylbilane synthase	1.1
310645	EOS10576	AI420742	Hs.163502	ESTs	1.1
332238	EOS32169	N53480	Hs.108622	ESTs	1.1
300966	EOS00897	AA564740	Hs.258401	ESTs	1.1
330437	EOS30368	HG2730-HT2827		Fibrinogen, A Alpha Polypeptide, Alt. Splice 2, E	1.1

302292	EOS02223	AF067797		EST cluster (not in UniGene) with exon hit	1.1
330138	EOS30069	c21_p2 gi|4210430|emb| gn 1 - 22334 22460 ex 3 3 CDSf 16.56 127 105		CH.21_p2 gi|4210430	1.1
332952	EOS32883	CH22_176FG_48_8_LINK_EM:AC000097.GENSCAN.2-4		CH22_FGENES.48_8	1.1
319901	EOS19832	T77136	Hs.8765	RNA helicase-related protein	1.1
321166	EOS21097	AA411263	Hs.128783	ESTs	1.1
336227	EOS36158	CH22_3625FG_730_2_LINK_DA59H18.GENSCAN.36-2		CH22_FGENES.730_2	1.1
302332	EOS02263	AI833168	Hs.184507	Homo sapiens Chromosome 16 BAC clone CIT987SK-A-328A3	1.1
313800	EOS13731	AW296132	Hs.166674	ESTs	1.1
339356	EOS39287	CH22_8326FG__LINK_BA354I12.GENSCAN.31-1		CH22_BA354I12.GENSCAN.31-1	1.1
324512	EOS24443	AW502125		EST cluster (not in UniGene)	1.1
319235	EOS19166	F11330	Hs.177633	ESTs	1.1
320352	EOS20283	Y13323	Hs.145296	disintegrin protease	1.1
338316	EOS38247	CH22_6944FG__LINK_EM:AC005500.GENSCAN.304-2		CH22_EM:AC005500.GENSCAN.304-2	1.1
333964	EOS33895	CH22_1241FG_305_2_LINK_EM:AC005500.GENSCAN.164-2		CH22_FGENES.305_2	1.1
312758	EOS12689	AA721107	Hs.202604	ESTs	1.1
338178	EOS38109	CH22_6726FG__LINK_EM:AC005500.GENSCAN.219-6		CH22_EM:AC005500.GENSCAN.219-6	1.1
315199	EOS15130	AA877996	Hs.125376	ESTs	1.1
312321	EOS12252	R66210	Hs.186937	ESTs	1.1
338765	EOS38696	CH22_7588FG__LINK_EM:AC005500.GENSCAN.518-1		CH22_EM:AC005500.GENSCAN.518-1	1.1
330547	EOS30478	U32989	Hs.183671	tryptophan 2;3-dioxygenase	1.1
315368	EOS15299	AW291563	Hs.152495	ESTs	1.1
328691	EOS28622	c_7_hs gi|6588001|ref| gn 7 - 579598 579664 ex 2 3 CDSi 12.78 67 4326		CH.07_hs gi|6588001	1.1
329179	EOS29110	c_x_hs gi|5868704|ref| gn 2 + 181639 181815 ex 3 4 CDSi 0.32 177 1939		CH.X_hs gi|5868704	1.1
327072	EOS27003	c21_hs gi|6531965|ref| gn 55 - 3796429 3797197 ex 4 4 CDSf 9.33 769 1270		CH.21_hs gi|6531965	1.1
312056	EOS11987	T83748	Hs.189712	ESTs	1.1
339128	EOS39059	CH22_8046FG__LINK_DA59H18.GENSCAN.55-2		CH22_DA59H18.GENSCAN.55-2	1.1
307646	EOS07577	AI302236		EST singleton (not in UniGene) with exon hit	1.1
319198	EOS19129	F07354		EST cluster (not in UniGene)	1.1
338556	EOS38487	CH22_7283FG__LINK_EM:AC005500.GENSCAN.417-8		CH22_EM:AC005500.GENSCAN.417-8	1.1
306143	EOS06074	AA916314		EST singleton (not in UniGene) with exon hit	1.1
332384	EOS32315	M11433	Hs.101850	*retinol-binding protein 1; cellular*	1.1
325100	EOS25031	T10265	Hs.116122	ESTs; Weakly similar to coded for by C. elegans cDNA yk30b3.5 [C.elegans]	1.1
309839	EOS09770	AW296076		EST singleton (not in UniGene) with exon hit	1.1
312180	EOS12111	AI248285	Hs.118348	ESTs	1.1
330385	EOS30316	AA449749	Hs.31386	ESTs; Highly similar to secreted apoptosis related protein 1 [H.sapiens]	1.1
315882	EOS15813	AI831297	Hs.123310	ESTs	1.1
325843	EOS25774	*c16_hs gi|6552453|ref| gn 1 - 7126 7232 ex 1 3 CDSI 1.87 107 182*		CH.16_hs gi|6552453	1.1
330783	EOS30714	D60050	Hs.34812	ESTs	1.1
317224	EOS17155	D56760	Hs.8122	ESTs	1.1
316042	EOS15973	AW297979	Hs.170698	ESTs	1.1
333524	EOS33455	CH22_781FG_175_10_LINK_EM:AC005500.GENSCAN.53-15		CH22_FGENES.175_10	1.1
302357	EOS02288	X03178	Hs.198246	group-specific component (vitamin D binding protein)	1.1
309830	EOS09761	AW294725		EST singleton (not in UniGene) with exon hit	1.1
321489	EOS21420	AW392474	Hs.172759	ESTs; Moderately similar to !!!! ALU SUBFAMILY SQ WARNING ENTRY !!!! [H.sapiens]	1.1
312304	EOS12235	AA491949	Hs.183359	ESTs	1.1
322026	EOS21957	AA233527	Hs.213289	low density lipoprotein receptor (familial hypercholesterolemia)	1.1

TABLE 1A

Table 1A shows the accession numbers for those primekeys in Table 1 which lack a unigeneID. Listed for each probeset is the gene cluster (CAT) number from which the oligonucleotides were designed. Gene clusters were compiled using sequences derived from Genbank ESTs and mRNAs. These sequences were clustered based on sequence similarity using Clustering and Alignment Tools (DoubleTwist, Oakland California). The Genbank accession numbers for sequences comprising each cluster are listed in the "Accession" column.

Pkey: Unique Eos probeset identifier number
CAT number: Gene cluster number
Accession: Genbank accession numbers

Pkey	CAT number	Accession
300611	337193_1	N75450 AA877636 AW137945 W05248 AA514763 AW972399 AI758397 AW195051
301187	434061_1	AW976692 AA806542 AA745856
301254	463589_1	AI049624 AA814705 AW404856 BE078289 BE078292
301266	468223_1	AA829774 AI082020
301454	534162_2	AI751738 AA977930
301615	5613_2	W39477 AK002047 NM_015515 T58707 AA386214 C19007 AA295466 T49621 T47323
301661	7974_1	AK001735 AF227906 AI815558 AW238991 AL133051 AW272417 AI083492 AI816503 AW888717 AA333166 AI925832 BE048352 BE048415 AI141922 AW805674 AW805578 AA633581 AA424632 R71439 AW020988 AW976735 AA883247 W37208 AI091039 AW317020 BE221788 AA502917 AW009024 AI141417 BE349081 AI421443 AI080490 AI003921 AI373690 AI379240 AA424587 AA740607 AA972391 AA620797 AW271656 AA400517 AI370902 AI680616 AA757270 AA909500 N32107 R43738 AI270464 AI870568 AI085139 AA225666 Z41046 AI767739 AI270546 N56779
301685	326972_1	W67730 Z44630 AA490699 W67596 W76661 R21207
301804	61_1	AK001468 AA190315 AA374980 AW961179 AA307782 AA315295 AA347194 AW953073 AW368190 AW368192 AA280772 AA251247 N85676 AI215522 AI216389 N87835 R12261 R57094 AI660045 AA347193 R16712 AW119006 N55905 N87768 AW900167 AI341261 AI818674 D20285 AI475165 AA300756 R40626 AI122827 AA133250 AI952488 AA970372 AA889845 AW069517 AI524385 AA190314 AI673359 AA971105 AI351088 AI872789 AI919056 AI611216 AK001472 BE568761 AA581004
301976	128835_1	T97905 AA101672
302245	9482_1	H18835 R47363 AI460004 N31660 AA454774 AA551759 AI417040 AA694490 AA633315 AI344661 AA708532 AA878567 AI802702 AI913465 AW001160 AA932133 AI092908 AA026974 AW628573 AA592910 H18836 AI274428 C00675 AK000048 BE313619
302292	27735_1	AF067797 AB013456 NM_001169 AI791955 AW843925 AI732659 AA577625 AW083143 AW138645
302476	31932_3	AF182294 NM_016200 AL046942 AI354410 AI697029 AI859557 AW188855 AW105437 AI358735 AW000959 AI491813 AW023693
302623	9705_1	AW836724 BE243668 AB019571 H43803
302626	10441_1	AK001553 AK001951 AB021870 NM_016282 F01168 AA211870 AA078889 AA312979 AL138385 R70844 AA165658 AA007279 AA194688 H65871 AA476639 F01095 AA300170 R39487 AA649126 AA193643 AA418300 BE173477 N84408 AW024465 AA406255 BE173412 BE173583 BE173470 AW069288 AA372937 BE504414 AA209472 AI262833 AI628359 AI458075 AI476266 AA397706 AI768605 AW243125 AI056436 AA838326 AA810651 AI472025 N35912 AA165622 AI985532 AI139528 AA626087 W16998 AI632833 AW130827 AW662551 AA731459 AW780188 AI653447 AI694970 AA810662 AI199987 AI587402 AI492972 H65872 AI805624 AW194835 AW994874 R70790 AA836506 N53285 F00181 R83595 AI290941 AW936750 AW936703 AW936623 AW936785 AW936691 AW936668 AW936713 AW936788 AW936744 AW936613 AW936614 AW936665 AW936702 AW936647 AW936643 AW936712 AW936791 AW936624 AW936672 AW936754 AW936696 AW936802 AW936792 AW936589 AW936692 AW936645 AW936746 AW936801 AW936748 AW936661 AW936612 AW936697 AW936704 AW936695 AW936626 AW936794 AW936629 AW936577 AW936798 T35617 AA375943 R29459 AW936717 AA342108 AW963351 Z24876 AW936708 AW374110 AW936586 W20080 AW936752 W31803 AA093709 AA431256 AW803610 AA424959 W76607 AA432267 W72009 R70817 AW778851 AA890563 AA194632 AI089644 AI373864 AA890333 AI745574 AI095714 AI567507 AI280712 AW864083 AW468991 N48087 AA860500 AA279471 AA993680 AA676504 AI360949 AI052134 AI038657 AI439836 AA629147 AA651840 AA435925 AA854457 AW796472 AA838729 AA193407 AA302403 AW958003 AA342107 AA639258 AI435811 AA410342 N25790 AA156454 AI539628 AI275854 N58849 AI858171 AW338576 W15321 AA418342 AA780577 W04701 AA630452 AW769154 AI274286 N23736 BE465020 AI554346 AI920804 AA969728 AW193440 AI368697 AA115096 AA564981 AA630461 N91475 BE464381 AA913741 AA757161 Z24907 C00067 AA649290 AI245223 AA363098 AI520754 AA887983 AI273015 AW878871 AW878981 AA480455 AA709267 AW959521 AW959523 N90014 N32441 F00193 AA115095 AA147583 W19813 AI333349 AI197937 R39488 AW750110
302655	41899_1	AJ227892 AA338715 BE074475 BE074469 BE074474 AW006182 AW572953 AI831725 AI762923 AI341466 AW449335 BE551686 AI692895 AI040410 AI276881 AI891008
302758	24028_3	AK001841 H40087 H11121 AW408676 N99603 AA984563 H92041 H11226
302882	458_60	AW403330 AF062097

302977	47403_3	AW263124 AI925166 AW105732 AA804479 BE621436 AF086399 W79085 W74440 AW992181 AA389686 AA314311 AA173955 AA677564 D59895 D60771 AI887733 C14814 AW162193 D81894 AA732538 AW150919 AA748064 AA769465 AA708143 BE327613 AA092726 AI692476 T35673 Z33600 AA134036 AI671394 AI267461 AW362795 AI769759 AA909042 AA130042 AW156938 AI753129 AI246205 AI823883 AI752836 D60770 AI336386 AI584003 AW627976 AI348676 D59894 AI969795 AW073259 AI400534 AI081318 AI082427 BE550515
302980	47495_1	AI925740 AF086489 W93435 W93345 AA337166 AW966214 AA336257 T11355 AW842435
303011	41689_1	AF090405 AF090407 AF090406
303037	35681_1	AF118395 NM_014317 AW376657 AW848189 AI261617 AI963829 AW848591 AW848598 AW376696 AW848523 AW848450 AW848655 AW848183 AW848550 AW376675 AI632752 AI590245 AI431824 AI857990 AI953341 AA888092 AW364968 AI188545 AI217741 AW275906 AI311481 AI991404 AI364963 AA628392 AA927982 AW150563 AA503063 AW079470 AW512180 AA889371 AW390132 AW609052 AW390112 AW581780
303042	5058_1	AW505345 AF129532 AF126028 AA852108 BE169359 R83701 Z43904 BE613543 AA283163 AA905463 AW067849 R13544 R12337 R14020 H98970 AI474918 N56139 AL135669 AW067702 AW372065 AW631389 AA083416 AA287511 AA602923 AA488914 AI167215 AW946829 R82855 AI948792 AA371333 AW953883 AW956152 C02539 AA298280 AI932587 AA022742 AI983021 AA195252 N58991 R78733 AW083996 H39614 AI365249 AW615389 AI927744 AI089971 N52205 AA083417 BE326666 BE349514 AI743785 AI640148 AI378211 AW181881 AI949484 W31374 AW628233 AA418406 AW068010 AI708085 AI092696 AI089823 AI277828 AA022660 AI440527 AW054937 AW474104 AI017436 AI159819 AI356716 AW473140 AW316518 N34522 AI675092 AI866697 AA864593 AW511185 AA488844 AA904975 N49111 Z39951 R37265 AI141362 T25856 R20664 F03163 AI767927 AA805942 D79905 AI914645 AW190553 AI934213 AI458796 AA195385 R82854 W31965
303072	4654_1	AI566718 AF157833 NM_012133 AI202415 AK002086 AF207598 AI214562 AI202184 AI865579 AA603481 AA483808 AA909166 AA774034 AW748102 AW176026 AW351472 BE164787 AA970983 BE622521 BE389817 AW366336 AW366328 AW366327 AW366329 AW366335 AW366337 BE269711 T11249 T11264 BE253295 BE256412 BE250882 BE255440 BE257663
303149	97393_1	AW963315 AA312995 AA037152 AA088607 AA064770 BE088067
303306	11887_1	AB037732 AW503898 AA215297 BE547488 AW177355 AA046224 AA361664 AA773328 AW512704 AI283330 AI307357 AI138263 AA046116 AI219874 AA315431 AW169999 AA492006 AW298002 AA043140 AA131781 AA292383 AA031721 AA027867 R31381 AW023352 AI686186 AW467416 AA493914 AA483019 AA483081 AA040871 AA558288 AW070397 AW572828 AA693439 AW206584 AA761354 AA907254 AI671019 BE221791 AI915828 AA744724 AA027815 AA131769 AA031641 AA837286 AA737401 AI765196 AW086076 AW873024 AI567164 AA744556 AA888910 AI572276
303443	224022_1	AA320525 AW025411 AI684617 AI653685
303502	325188_1	BE174240 AA488528 AL042253
303582	647662_1	AA377444 AI458965
303610	226089_1	BE247299 AA323288 AW966142 AA334916 AL046572 BE145095 AW751265
303642	284260_1	AW299459 AA417112
303777	244977_1	AA348491 BE246984 AW505247
303839	1770217_1	Z45939 T54414 T06550
303874	5013_1	AL050333 F08138 Z43325 H13393 AA258921 AA224232 BE439918 AL050018 AW363692 AA236615 AA746291 Z19312 AA428674 Z28579 T32527 AW952956 R59046 AA403173 AA403171 AW023058 AA461143 BE149531 AA428185 AI382812 H42659 AA406086 L48858 AW630177 Z24777 AW675297 AI393859 AI743022 AI669354 AW803015 AA401255 AI952901 AW043840 AI808787 AI140662 AA194627 AI140997 AA007454 AA007318 AI469859 AI540581 C06482 AI277356 AI458423 AA460839 AA861452 AI080197 AA630781 AA845367 AI125582 AA411705 AA970524 AA699910 AW804640 AW805007 AA724226 AI128207 AI696852 AW673064 AA748404 AW771788 AW088185 AI026976 AI537560 AA224233 T24024 T50208 AI827319 R17235 T11904 AI816830 R41845 AA639828 Z41214 AA258158 H06057 F02752
303886	81595_1	AW365963 BE141537 BE141535 BE141538 T19123 R57434 Z43870 AA298099 AA298004 AW963314 AI627790 AA298160 BE501485 AW271198 AA195563 AA195584 H28868 AA004370 Z42582 R21338
303929		AW470753
304084		T91986
304143	30606_-14	R88737
304165		H73265
304183		H91161
304236		W93278
304350		AA186871
304439		AA398882
304495		AA446448
304518		AA461438
304521		AA464716
304546	14011_1	AF113676 X01683 K01396 M11465 NM_000295 K02212 J02619 AB004044 H60588 T72131 T74637 T70970 T73183 T62154 R93629 H50855 H80585 H78044 T69186 R95698 H59327 T54018 H83071 R99626 H89864 H91798 T72841 T71108 T72812 T54005 T50896 H56102 W01486 W01669 AA137076 H90340 T61854 T61840 N93360 T61844 N53576 T55852 X02920 H56350 T58720 H56351 R92748 H56914 H59279 H50665 H56928 T69144 H80448 R91066 H77829 R92479 T55014 T52174 T67613 AA845231 H95664 V00496 M26123 AA484470 AI114833 T58716 T64752 T50876 T67858 H48675 T51161 T70409 T61715 T72289 H51854 H72171 T50834 H81483 T72132 T58792 T51179 T72833 R29662 T60563 W23562 H94193 T55017 T74830 H78469 H90811 T61303 H75867 T71527 T68360 R91065 R91079 T71172 H52923 T50871 T86567 H94691 T69226 AV649730 T46850 T56587 T46849 T60552 BE043578 BE042051 T72296 T61001 T58918 T52107 H82324 H47453 R06725 D16856 T48282 T52250 R92117 AI287339 H73203 AA318670 D17206 H66626 T69268 H73485 R93078 H73533 R87097 T71529 AA885254 AA486074 R94242 H74033 T73643 D12131 AV655901 AA345387 W07278 AW371443 AW371484 AW371427 AW371435 AW371467 AW371474 AW371471 AW371453 AW371448 AW371468 AW371486 AW371521 AW371463 AW371485 AW371460 T55283 H58030 H68955 AA360298 H73996 T58919 N94213 T50911 H51045 T56077 T72988 T71819 H60101 T72439 T68079 T73548 D11609 T61008 H67597 N49781 T73190 H50843 T73140 H61124 AV657376 N39304 AW075086 AI247165 H73123 H60258 AA343450 X17122 AW470706 AA336649 AW392737 H75576 N76963 T64227 AI803294 W73727 AV649563 AI307406 AW075080 D11525 AI032826
304547		AA486189
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322959	132817_1	AI267606 AA121045 AA126521
322968	17218_2	AI272141 AI879676 AF070669 W25179 AA534016 AA533386 AA010740 AF124147 W16493 W56636 AA258911 AA321677 H44503 AA642777 AA081800 W69885 H82507 AA536128 AA326782 AA326783 AA353693 AA354642 R73311 AA354400 W79820 W16502 AA301647 AI202303 AA453926 AA705795 AA011128 AA929033 AI393389 AA845133 AI445640 AI677727 AI818296 AI369820 AI539292 AI870541 W69797 AI871096 BE550803 N35853 AA644019 N27809 R49769 AA738197 AI565700 AW207656 AA587216 AA669237 AI906947 AI809956 AI740905 AW043811 AW182476 AA659844 AI742797 AI832103 AI660967 R86125 AI674667 AI808074 AI869284 AI336214 AI218002 AI338629 AI857930 AW183986 BE044333 AW135467 AI826077 AI357643 AI475486 AA478855 AW172550 AI553942 AA868731 AW268850 AI123793 AI887022 AA046935 AI361954 AI091737 AI682235 AI367076 AI088882 AI808682 AI312679 AA046955 AW027546 AI660019 AI696174 AW008626 AI266337 AI568959 AW027409 AI040014 AW134559 AA479953 AA910082 AI301458 AW028352 AI017863 AI268915 AI185866 AI265907 AI274195 AW051540 AW027515 AI380435 AA883117 AI279396 AA846628 AW628235 AW206201 AW628510 AA954276 AI301405 AI827185 AI553978 AI200301 AI470343 AA933953 AI914937 AI362849 AW085066 AI204021 AA631192 AI351701 AA748663 AA993806 AA580146 AW027744 AA580016 AA897344 AI042638 AI473196 AA995065 AW027720 AI217421 AI935604 AW449411 AW237094 AI653348 NM_003107 X70683 AI470473 AI765137 AI193479 AI253050 AI470510 AI399828 AI371461 AI185518 N20940 R49816 N79977 W56599 N24649 W78113 N78761 AI817673 AI911482 AW205984 AI240186 AI828016 AI942449 X65661 AW751587 AI392808 AI624192 AI950969 AA573260 AI203361 AI479942 BE041834 AW305351 AI918327 BE048713 AW071712 BE041565 AI139260 BE466360 BE502737 AW007819 AW071887 AI742130 AI344020 AW772112 AI932275 AI992189 AI197801 BE219990 AI990863 AI536934 AI336275 AI971955 AI798204 AI870429 AI652390 AI080187 BE219486 AI185434 AW628564 AW072399 AI656370 AI498606 BE041559 AI743591 AW515805 AI087833 AI917506 AI123191 AI858043 AI334046 AI242585 AI636670 AI919478 AW771487 AI417185 AI468527 AW137861 AI554782 AI130733 AW005164 AI910551 AI189135 AI963934 AI985482 AI660396 AI497963 AW204662 AW137602 AI382505 AI493485 AI185987 AI078841 AI830054 AI378223 AI351299 AA937301 AA242817 AA258359 AW027603 AI935204 AI500360 AI569741 BE551058 AW275536 AI457854 AI142093 AW028288 AI286002 AI279114 AI364121 AI341323 AI190436 AW002607 AI242488 AI338122 AI368600 AI340276 AI417994 AI190234 AI275527 AI934886 AI498274 AI813630 AI075339 AI087976 AI459251 AI989477 AW004046 AI992190 AI885279 AI479475 AI698030 AI473294 AI951648 AI699587 AI660602 AI873018 AW613987 AI808297 AW270159 AW572955 AW195908 AW469034 AW197100 AA885164 AW611668 AI143038 AI910560 AA418374 AW341092 AI871169 AI937136 AI204003 AA775707 AW590759 AW593350 AW572981 AI197905 AI660941 AI743469 AW237017 AI808587 AI984962 AA418254 AI828104 AA625231 AI832151 H84232 AI240215 AI911775 AI219668 AI336801 AA232630 AI343471 W69129 N93602 AA768883 W04386 AI086277 AA983433 W07646 AA458584 N86625 AI384055 AI928089 W25479 AA242952 AI763303 AI225039 AI740896 AA953758 W69240 AA558331 AI760593 AA558712 AW992121 AW992157 W69115 BE328596 AI953190 W95311 AI950195 AI739605 AI857262 W69185 AA884586 AI198104 AI127451 AA905932 AA723310 AI936623 AA732940 AI332918 AI221396 AI336095 AI200067 AI824853 D55893 D52697 D56205 AA232764 T53299 H84555 AA076539 AA158347 BE298430 AL134493 AW732398 AW750740 AW578208 N36572 AA453861 AA252914 AA234197 AW576988 AW577034 AA025199 AW577052 AW385538 AW576996 AW577021 T83230 AA421529 AI918492 AA909038 AA507060 AA654561 AA064597 AW001594 AW469192 AI368002 AI142435 AW379382 W93438 AA076387 AI802344 AI097013 AA987215 AA635282 W93349 AI017818 AA421564 AA158348 AI140004 AA506259 AW473184 AA236350 AI138669 H96873 AA974889 AA643735 AA995463 AA995471 AA809555 AA253225 AI298682 AI572515 T53300 AA064596 AA193589 AA025118 AI669682 AA610638 T90774 AI972332 AI280776 T27980 AW136058 BE000428 AI378691 AA961520 BE049142 AI311424 AA283211 AI344071 AI344007 AI344097 AI582410 AL036314 AW798038 AI905228 C15325 AA380386 AW958417 AW630531 BE538239 T70488 AA088296 T34175 T31626 D54331 D53142 AA029415 AW946823 AI914128 AA355446 T34322 BE006559 M85677 AA034335 T31463 AW804007 AA256591 D55128 AI535884 D55192 N23605 T31802 AA326899 AW999156 AA355201 AW999306 AI091590 BE172021 AA029490 BE000255 AW339939 AW150093 AI872098 AI274876 T06303 AA857909 N23606 AA922714 AI914104 AI285281 AW999919 AI339803 AI081354 AA972184 AI049566 AW151583 AI682455 AA088257 AI217050 BE551774 AI277033 AI252627 AA910406 AI369422 H46634 AI873113 AA033710 AW078579 AI636452 N23010 AA357263 AA256592 T05786 AA884195 AA406145 AA907807 AA482840 AI637691 AA654523 AA911495 T06601 AW594370 AW016524 C15324 AA622519 AA340191 AA174168 C13992 T69433 T96576 AW166622 T96575
323011	139750_1	AA580288 AA315655 AA133031 AA377748
323166	162676_1	AA291001 AA188974 AA290616
323216	6526_1	AA332145 AA331790 AW962563 AA868189 L13837 T34468 AA055882 AA096148 AA092327 H57062 R59098 R11247 F07659 Z44949 AF131829 L13835 T79889 AA252451 N28984 H85260 AL046384 AW995631 R58386 AI061651 AW376050 AW379789 W90347 AA450157 AI799939 AA461340 W02347 AA233095 N39675 AA659441 AW995284 W17060 R32252

		AI042599 AL046385 AI970370 AA744764 AI249761 AI628106 R32668 AI863011 AI923998 AI186798 N26601 AI141864 N34992 AI377031 N23934 AI683466 BE219548 AA622032 AW089867 AA243717 N79547 R59099 AW241293 AI917545 AW103697 AI383179 AW517527 AW193642 W90348 AW381409 R11195 AA461166 AA836624 AA280285 AW242055 L13836 N89647 L13834 AI358605 AA452023 AI868391 H57063 AW075868 N20590 Z40695 R37603 R28484 AA251913 F03914 AA055772 N43752
323243	140566_2	W47525 AA134047 BE391212 AA330333 AA376355 BE304871 BE167342 H87402 AA631722 W45724 AA715517 AI925438 AI804849 AW241617 AW403807 AI653435 AA134048 AW747874 AI922327 AI814967 AI935895 AA228865 AW504076 AA225008 AW673858 C03914
323244	647858_1	AW675572 AI248270 T85161 AL133848 T70731 T69747
323333	62251_1	AV651680 AA228883 AA367341 AW962458 AA628024 AW172426 AI767785 AA313012 AW963323
323430	63341_1	AW062479 AW062488 AW062491 AW062480 AW938564 AW062478 AA322408 AA324351 AW938595 AW938598 BE162389 AW176556 AW938599 AW838792 AW938566 BE162305 BE162377 AW938570 AW062459 AW176555 AW938562 AW938568 AA251701 BE162320 AW938597
323465	193343_1	AA287406 AA261844 AA261845 AA287355 AA810895
323479	194627_1	AA278246 AW292815 AA278703
323538	217887_1	AW247696 BE265140 AW403615 AL037647 AA312336
323632	333100_1	AL041844 AL040002 AL039950
323731	226193_1	AA323414 AW664013 AI809377 AI276041 AW296883 AI798340
323753	12462_4	AK002161 AA327102 AI056868 AI743901 AI139018 AI199114 AI076003
323835	506747_1	AL042005 AL042006 AA911481
323898	243407_1	AA347566 AA346521 AI111169
324048	267284_1	AA378739 AW964174 AA570564 AI076833 AW265063 AW006805 AA480656 AW004789
324231	975669_1	W60827 AL079968 AL047234
324430	312113_1	AA464018 AA464079 AA468142
324432	312487_1	AA464510 AA631257 AI740516 AI739132 AW972467 AI741376 AW068935 AI467852 AI752240 AI123717 AI754551 AW205510 AW044211 AW028889 AW198033 AI538632 AA513096
324456	1155396_1	AW500954 AW501111 AW501394
324512	1156071_1	AW502122 AW502125 AW501663 AW501720
324575	65704_1	AW502257 AI014241 AA100360 BE298534
324609	333046_1	AW299534 AW299896 AA504765 AA505099 AA505100 AA584753 AW136415 AA768306
324620	69834_1	BE397649 H14413 BE397689 BE514098 H53372 AA448021 R57944 AI307272 BE259369 H72331 BE251092 T27364 AA001666 AA044433 AA875998 AW075405 AW338356 AA001667 AW300173 AW514944 AW468914 AA604673 AA702749 AA805550 AA447621 AA934104 AI373527 AA604794 AI911203 AI500644 AI291383 AA731133 BE350633 AA044604 H95689 H14366 AV660983 AA912893 AI369587 AI382271 AA917508 AW138391 BE622560
324662	560496_1	AI376331 AI819150 AI097038 AI351100 AW504689
324670	72231_1	AW503713 AA352950 AA044972 BE618246 AA335047 AW962269
324692	351987_1	AA557952 AA677593 AA618150
324715	290035_2	AI739168 AA426249 AI199636 AW505198 AW977291 AA824583 AA883419 AA724079 AI015524 AI377728 AW293682 AI928140 AA731438 AI092404 AI085630 AA731340
324728	210991_2	T85872 T48305
324783	389615_1	AA640770 AI683112 AA913009
324848	371388_1	AA602539 D59262 AI684171 N46711 AW021857 D19768
324961	376239_1	AA613792 AW182329 T05304 AW858385
324988	22162_1	AK001379 AK001411 AW795711 T06997 AA287540 AA354538 AW957773 AI632268 AI651003 AI689650 AI809332 AW304483 AI805269 AA278506 AA862381 AA287875 AW628545 AI085761 AW025965 AI658615 AW628879 AW139496 AI214278 AA902745 AA991679 BE540102 AW593658 AI745602 AA744687 AI285441 AA807089 AI218314 AA721449 AI202987 AA432129 AI285502 AI281462 AA731319 BE082573
325071	1562044_1	H09693 H09699 T09229
325176	700767_1	T19142 AI351168 T52843 BE241963

TABLE 1B

Table 1B shows the genomic positioning for those primekeys in Table 1 that lack unigene ID's and accession numbers. For each predicted exon, the genomic sequence source used for prediction is listed. Nucleotide locations of each predicted exon are also listed.

Pkey: Unique number corresponding to an Eos probeset
Ref: Sequence source. The 7 digit numbers in this column are Genbank Identifier (GI) numbers. "Dunham I. et al." refers to the publication entitled "The DNA sequence of human chromosome 22." Dunham I. et al., Nature (1999) 402:489-495.
Strand: Indicates DNA strand from which exons were predicted.
Nt_position: Indicates nucleotide positions of predicted exons.

Pkey	Ref	Strand	Nt_position
332792	Dunham, I. et.al.	Plus	73381-73768
332908	Dunham, I. et.al.	Plus	1934283-1934366
332909	Dunham, I. et.al.	Plus	1946582-1946735
332913	Dunham, I. et.al.	Plus	1963539-1963843
332952	Dunham, I. et.al.	Plus	2472864-2473012
332958	Dunham, I. et.al.	Plus	2516164-2516310
332961	Dunham, I. et.al.	Plus	2521424-2521555
332975	Dunham, I. et.al.	Plus	2599641-2599702
332991	Dunham, I. et.al.	Plus	2686938-2687372
333119	Dunham, I. et.al.	Plus	3288316-3288640
333131	Dunham, I. et.al.	Plus	3350064-3350170
333139	Dunham, I. et.al.	Plus	3369495-3369571
333156	Dunham, I. et.al.	Plus	3617584-3617790
333222	Dunham, I. et.al.	Plus	3979706-3979803
333254	Dunham, I. et.al.	Plus	2521424-2521555
333348	Dunham, I. et.al.	Plus	4711908-4712181
333349	Dunham, I. et.al.	Plus	4713940-4714084
333366	Dunham, I. et.al.	Plus	4798273-4798469
333384	Dunham, I. et.al.	Plus	4907535-4907610
333385	Dunham, I. et.al.	Plus	4907928-4908032
333391	Dunham, I. et.al.	Plus	4916697-4916780
333488	Dunham, I. et.al.	Plus	5396233-5396310
333520	Dunham, I. et.al.	Plus	5586133-5586296
333524	Dunham, I. et.al.	Plus	5612620-5612780
333532	Dunham, I. et.al.	Plus	5622804-5622937
333580	Dunham, I. et.al.	Plus	6142935-6143145
333585	Dunham, I. et.al.	Plus	6234778-6234894
333597	Dunham, I. et.al.	Plus	6331421-6331536
333619	Dunham, I. et.al.	Plus	6562799-6562926
333671	Dunham, I. et.al.	Plus	7038849-7039193
333680	Dunham, I. et.al.	Plus	7071730-7071794
333682	Dunham, I. et.al.	Plus	7076641-7076760
333763	Dunham, I. et.al.	Plus	7692491-7692630
333764	Dunham, I. et.al.	Plus	7693573-7693716
333769	Dunham, I. et.al.	Plus	7696625-7696707
333770	Dunham, I. et.al.	Plus	7700384-7700476
333849	Dunham, I. et.al.	Plus	8018323-8018472
333875	Dunham, I. et.al.	Plus	8135505-8136179
333882	Dunham, I. et.al.	Plus	8153002-8153169
333922	Dunham, I. et.al.	Plus	8381385-8381444
333928	Dunham, I. et.al.	Plus	8468844-8469015
333947	Dunham, I. et.al.	Plus	8579888-8579966
333949	Dunham, I. et.al.	Plus	8589634-8589791
333968	Dunham, I. et.al.	Plus	8681004-8681241
333983	Dunham, I. et.al.	Plus	8813593-8813668
333995	Dunham, I. et.al.	Plus	8855296-8855424
333997	Dunham, I. et.al.	Plus	8866668-8867255
334003	Dunham, I. et.al.	Plus	8892882-8892970
334012	Dunham, I. et.al.	Plus	9007456-9010221
334047	Dunham, I. et.al.	Plus	9428152-9428211
334063	Dunham, I. et.al.	Plus	9731991-9732085
334066	Dunham, I. et.al.	Plus	9739568-9739680
334078	Dunham, I. et.al.	Plus	9809783-9809863
334118	Dunham, I. et.al.	Plus	10344273-10344384

334122	Dunham, I. et.al.	Plus	10411792-10411901
334150	Dunham, I. et.al.	Plus	10529221-10529854
334220	Dunham, I. et.al.	Plus	12718720-12718857
334298	Dunham, I. et.al.	Plus	13424763-13425914
334324	Dunham, I. et.al.	Plus	13539210-13539323
334335	Dunham, I. et.al.	Plus	13608488-13608705
334433	Dunham, I. et.al.	Plus	14273261-14273429
334532	Dunham, I. et.al.	Plus	14792798-14792901
334561	Dunham, I. et.al.	Plus	14987299-14987447
334616	Dunham, I. et.al.	Plus	15176123-15176470
334628	Dunham, I. et.al.	Plus	15310346-15310415
334630	Dunham, I. et.al.	Plus	15322614-15322744
334631	Dunham, I. et.al.	Plus	15325949-15326116
334661	Dunham, I. et.al.	Plus	15477716-15477786
334677	Dunham, I. et.al.	Plus	15517449-15517560
334696	Dunham, I. et.al.	Plus	15665919-15666002
334714	Dunham, I. et.al.	Plus	15760702-15760767
334718	Dunham, I. et.al.	Plus	15775491-15775599
334720	Dunham, I. et.al.	Plus	15792931-15793085
334727	Dunham, I. et.al.	Plus	15942616-15942750
334739	Dunham, I. et.al.	Plus	16004120-16004225
334740	Dunham, I. et.al.	Plus	16009324-16009547
334769	Dunham, I. et.al.	Plus	16170704-16170876
334872	Dunham, I. et.al.	Plus	19162417-19162565
334876	Dunham, I. et.al.	Plus	19185336-19185400
334883	Dunham, I. et.al.	Plus	19223107-19223253
334891	Dunham, I. et.al.	Plus	19299770-19299944
334900	Dunham, I. et.al.	Plus	19315678-19315743
334902	Dunham, I. et.al.	Plus	19317083-19317195
334914	Dunham, I. et.al.	Plus	19495158-19495275
334916	Dunham, I. et.al.	Plus	19572924-19573846
335044	Dunham, I. et.al.	Plus	20842088-20842682
335081	Dunham, I. et.al.	Plus	21113871-21113937
335158	Dunham, I. et.al.	Plus	21569610-21569666
335164	Dunham, I. et.al.	Plus	21585912-21586014
335166	Dunham, I. et.al.	Plus	21587100-21587213
335170	Dunham, I. et.al.	Plus	21623383-21623967
335188	Dunham, I. et.al.	Plus	21669118-21669328
335189	Dunham, I. et.al.	Plus	21673403-21673472
335200	Dunham, I. et.al.	Plus	21743499-21743881
335211	Dunham, I. et.al.	Plus	21774611-21774680
335219	Dunham, I. et.al.	Plus	21875591-21875688
335221	Dunham, I. et.al.	Plus	21882840-21882968
335225	Dunham, I. et.al.	Plus	21890315-21890448
335255	Dunham, I. et.al.	Plus	22032258-22032661
335287	Dunham, I. et.al.	Plus	22299047-22299299
335361	Dunham, I. et.al.	Plus	22807292-22807445
335364	Dunham, I. et.al.	Plus	22833430-22833586
335369	Dunham, I. et.al.	Plus	22843392-22843506
335468	Dunham, I. et.al.	Plus	23787245-23787367
335481	Dunham, I. et.al.	Plus	24082522-24084870
335488	Dunham, I. et.al.	Plus	24118744-24118839
335496	Dunham, I. et.al.	Plus	24164386-24164545
335497	Dunham, I. et.al.	Plus	24167666-24167869
335499	Dunham, I. et.al.	Plus	24176698-24176869
335504	Dunham, I. et.al.	Plus	24182110-24182199
335599	Dunham, I. et.al.	Plus	25043628-25043775
335623	Dunham, I. et.al.	Plus	25138489-25138547
335653	Dunham, I. et.al.	Plus	25329710-25329802
335687	Dunham, I. et.al.	Plus	25445952-25446064
335690	Dunham, I. et.al.	Plus	25455442-25455625
335692	Dunham, I. et.al.	Plus	25468557-25468725
335697	Dunham, I. et.al.	Plus	25481456-25481649
335701	Dunham, I. et.al.	Plus	25513366-25513807
335708	Dunham, I. et.al.	Plus	25541777-25541907
335739	Dunham, I. et.al.	Plus	25698550-25698826
335742	Dunham, I. et.al.	Plus	25712654-25712771
336003	Dunham, I. et.al.	Plus	28406289-28406759
336015	Dunham, I. et.al.	Plus	28640586-28640673
336016	Dunham, I. et.al.	Plus	28646816-28646947
336018	Dunham, I. et.al.	Plus	28660880-28660978
336019	Dunham, I. et.al.	Plus	28663992-28664102
336020	Dunham, I. et.al.	Plus	28683778-28683851
336021	Dunham, I. et.al.	Plus	28686482-28686559
336023	Dunham, I. et.al.	Plus	28698240-28698343

336071	Dunham, I. et.al.	Plus	29264457-29264684
336090	Dunham, I. et.al.	Plus	29413020-29413162
336107	Dunham, I. et.al.	Plus	29987731-29987869
336121	Dunham, I. et.al.	Plus	30048054-30048129
336124	Dunham, I. et.al.	Plus	30053441-30053500
336132	Dunham, I. et.al.	Plus	30107247-30107412
336135	Dunham, I. et.al.	Plus	30123235-30123335
336194	Dunham, I. et.al.	Plus	30443138-30443282
336235	Dunham, I. et.al.	Plus	31122315-31122623
336367	Dunham, I. et.al.	Plus	33942937-33943058
336379	Dunham, I. et.al.	Plus	33995071-33995243
336439	Dunham, I. et.al.	Plus	34186130-34186215
336502	Dunham, I. et.al.	Plus	34268953-34269083
336572	Dunham, I. et.al.	Plus	34446383-34446496
336602	Dunham, I. et.al.	Plus	13424060-13424582
336721	Dunham, I. et.al.	Plus	3371522-3371586
336739	Dunham, I. et.al.	Plus	2599641-2599702
336766	Dunham, I. et.al.	Plus	4905608-4905684
336833	Dunham, I. et.al.	Plus	6856506-6856634
336836	Dunham, I. et.al.	Plus	7077262-7077326
336878	Dunham, I. et.al.	Plus	9200300-9200399
336880	Dunham, I. et.al.	Plus	9250034-9250123
336902	Dunham, I. et.al.	Plus	10385555-10386053
336917	Dunham, I. et.al.	Plus	11228329-11228403
336919	Dunham, I. et.al.	Plus	11351181-11351274
336924	Dunham, I. et.al.	Plus	11525273-11525527
336946	Dunham, I. et.al.	Plus	12337073-12337258
336953	Dunham, I. et.al.	Plus	12988791-12988889
336979	Dunham, I. et.al.	Plus	14270748-14270816
337169	Dunham, I. et.al.	Plus	23529987-23530214
337175	Dunham, I. et.al.	Plus	23782209-23782374
337182	Dunham, I. et.al.	Plus	23934889-23934962
337238	Dunham, I. et.al.	Plus	27141465-27141776
337303	Dunham, I. et.al.	Plus	29128849-29128974
337489	Dunham, I. et.al.	Plus	33295724-33295872
337503	Dunham, I. et.al.	Plus	33385583-33385857
337504	Dunham, I. et.al.	Plus	33386053-33386236
337570	Dunham, I. et.al.	Plus	359309-359459
337585	Dunham, I. et.al.	Plus	951744-952008
337629	Dunham, I. et.al.	Plus	2017380-2017517
337670	Dunham, I. et.al.	Plus	3110593-3110760
337674	Dunham, I. et.al.	Plus	3332616-3332697
337692	Dunham, I. et.al.	Plus	3575105-3575299
337740	Dunham, I. et.al.	Plus	3870165-3870223
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325482	5866957	Plus	47957-48078
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328152	5868060	Minus	73981-74203
328170	5868071	Plus	93170-93295
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328251	6381891	Plus	124444-124557
328253	6381894	Minus	4411-4509
328084	6469819	Minus	155366-155459
328274	5868219	Minus	31244-31439
328615	5868239	Plus	35214-35347
328632	5868247	Plus	76734-76853
328779	5868309	Plus	41570-41639
328783	5868309	Minus	73658-73822
328801	5868321	Minus	44492-44609
328820	5868330	Plus	90446-90602
328835	5868339	Plus	88053-88461
328290	5868363	Minus	127366-127496
328321	5868373	Minus	1029614-1029673
328332	5868375	Plus	280154-280289
328333	5868375	Plus	282506-282664
328349	5868383	Minus	260704-260804
328450	5868425	Minus	209192-209321
328466	5868434	Minus	15643-15900
328479	5868449	Minus	331-560
328481	5868449	Minus	8987-9180
328546	5868487	Minus	17547-17722
328662	6004473	Plus	1184773-1184855
328767	6017031	Minus	35625-35723
328768	6017031	Minus	223741-224238
328857	6381927	Minus	80557-81051
328878	6552423	Plus	105580-105774
328882	6552423	Minus	157669-157826
328690	6588001	Minus	571207-571274
328691	6588001	Minus	579598-579664
330307	4877982	Plus	107384-107559
328903	5868514	Plus	23625-24468
328987	5868535	Minus	25705-25764
328998	5868538	Plus	40996-41104
329062	5868590	Minus	58977-59094
329086	5868604	Minus	35489-35588
329154	5868686	Minus	200851-201356
329156	5868686	Minus	202013-202341
329164	5868691	Plus	62305-62517
329170	5868693	Plus	67924-68019
329179	5868704	Plus	181639-181815
329193	5868716	Plus	168095-168181
329254	5868733	Plus	4133-4214
329369	5868842	Minus	121148-121516
329367	5868842	Minus	87201-87587
329141	6017060	Plus	343924-343997
329347	6456785	Plus	18433-18897
329017	6682532	Minus	255591-255672
329434	5868883	Minus	31124-31263

TABLE 2 DNA AND PROTEIN SEQUENCES FOR CBF9 AND BFO8

Table 2 provides the nucleic acid and protein sequence of the CBF9 and BFO8 genes as well as the Unigene and Exemplar accession numbers for CBF9 and BFO8.

CBF9 DNA SEQUENCE

```
Gene name:                    ESTs
Unigene number:               Hs.157601
Probeset Accession #:         W07459
Nucleic Acid Accession #:     AC005383
Coding Sequence:              328-2751 (underlined sequences correspond to start and
                              stop codons)
```

```
1          11         21         31         41         51
|          |          |          |          |          |
GACAGTGTTC GCGGCTGCAC CGCTCGGAGG CTGGGTGACC CGCGTAGAAG TGAAGTACTT   60
TTTTATTTGC AGACCTGGGC CGATGCCGCT TTAAAAAACG CGAGGGGCTC TATGCACCTC  120
CCTGGCGGTA GTTCCTCCGA CCTCAGCCGG GTCGGGTCGT GCCGCCCTCT CCCAGGAGAG  180
ACAAACAGGT GTCCCACGTG GCAGCCGCGC CCCGGGCGCC CCTCCTGTGA TCCCGTAGCG  240
CCCCCTGGCC CGAGCCGCGC CCGGGTCTGT GAGTAGAGCC GCCCGGGCAC CGAGCGCTGG  300
TCGCCGCTCT CCTTCCGTTA TATCAACATG CCCCCTTTCC TGTTGCTGGA GGCCGTCTGT  360
GTTTTCCTGT TTTCCAGAGT GCCCCCATCT CTCCCTCTCC AGGAAGTCCA TGTAAGCAAA  420
GAAACCATCG GGAAGATTTC AGCTGCCAGC AAAATGATGT GGTGCTCGGC TGCAGTGGAC  480
ATCATGTTTC TGTTAGATGG GTCTAACAGC GTCGGGAAAG GGAGCTTTGA AAGGTCCAAG  540
CACTTTGCCA TCACAGTCTG TGACGGTCTG GACATCAGCC CCGAGAGGGT CAGAGTGGGA  600
GCATTCCAGT TCAGTTCCAC TCCTCATCTG GAATTCCCCT TGGATTCATT TTCAACCCAA  660
CAGGAAGTGA AGGCAAGAAT CAAGAGGATG GTTTTCAAAG GAGGGCGCAC GGAGACGGAA  720
CTTGCTCTGA AATACCTTCT GCACAGAGGG TTGCCTGGAG GCAGAAATGC TTCTGTGCCC  780
CAGATCCTCA TCATCGTCAC TGATGGGAAG TCCCAGGGGG ATGTGGCACT GCCATCCAAG  840
CAGCTGAAGG AAAGGGGTGT CACTGTGTTT GCTGTGGGGG TCAGGTTTCC CAGGTGGGAG  900
GAGCTGCATG CACTGGCCAG CGAGCCTAGA GGGCAGCACG TGCTGTTGGC TGAGCAGGTG  960
GAGGATGCCA CCAACGGCCT CTTCAGCACC CTCAGCAGCT CGGCCATCTG CTCCAGCGCC 1020
ACGCCAGACT GCAGGGTCGA GGCTCACCCC TGTGAGCACA GGACGCTGGA GATGGTCCGG 1080
GAGTTCGCTG GCAATGCCCC ATGCTGGAGA GGATCGCGGC GGACCCTTGC GGTGCTGGCT 1140
GCACACTGTC CCTTCTACAG CTGGAAGAGA GTGTTCCTAA CCCACCCTGC CACCTGCTAC 1200
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GCCGTGCTGA GCGAGGACTC TCGGGCCCGA GTGGGTGTGG CCACATACAG CAGGGAGCTG 1500
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CGTGGCTTCG GGAGCGCCAC CAGGACAGGC CAGGACCGGC CACGTAGAGT GGTGGTTTTG 1680
CTCACTGAGT CACACTCCGA GGATGAGGTT GCGGGCCCAG CGCGTCACGC AAGGGCGCGA 1740
GAGCTGCTCC TGCTGGGTGT AGGCAGTGAG GCCGTGCGGG CAGAGCTGGA GGAGATCACA 1800
GGCAGCCCAA AGCATGTGAT GGTCTACTCG GATCCTCAGG ATCTGTTCAA CCAAATCCCT 1860
GAGCTGCAGG GGAAGCTGTG CAGCCGGCAG CGGCCAGGGT GCCGGACACA AGCCCTGGAC 1920
CTCGTCTTCA TGTTGGACAC CTCTGCCTCA GTAGGGCCCG AGAATTTTGC TCAGATGCAG 1980
AGCTTTGTGA GAAGCTGTGC CCTCCAGTTT GAGGTGAACC CTGACGTGAC ACAGGTCGGC 2040
CTGGTGGTGT ATGGCAGCCA GGTGCAGACT GCCTTCGGGC TGGACACCAA ACCCACCCGG 2100
GCTGCGATGC TGCGGGCCAT TAGCCAGGCC CCCTACCTAG GTGGGGTGGG CTCAGCCGGC 2160
ACCGCCCTGC TGCACATCTA TGACAAAGTG ATGACCGTCC AGAGGGGTGC CCGGCCTGGT 2220
GTCCCCAAAG CTGTGGTGGT GCTCACAGGC GGGAGAGGCG CAGAGGATGC AGCCGTTCCT 2280
GCCCAGAAGC TGAGGAACAA TGGCATCTCT GTCTTGGTCG TGGGCGTGGG GCCTGTCCTA 2340
AGTGAGGGTC TGCGGAGGCT TGCAGGTCCC CGGGATTCCC TGATCCACGT GGCAGCTTAC 2400
GCCGACCTGC GGTACCACCA GGACGTGCTC ATTGAGTGGC TGTGTGGAGA AGCCAAGCAG 2460
CCAGTCAACC TCTGCAAACC CAGCCCGTGC ATGAATGAGG GCAGCTGCGT CCTGCAGAAT 2520
GGGAGCTACC GCTGCAAGTG TCGGGATGGC TGGGAGGGCC CCCACTGCGA GAACCGTGAG 2580
TGGAGCTCTT GCTCTGTATG TGTGAGCCAG GGATGGATTC TTGAGACGCC CCTGAGGCAC 2640
ATGGCTCCCG TGCAGGAGGG CAGCAGCCGT ACCCCTCCCA GCAACTACAG AGAAGGCCTG 2700
GGCACTGAAA TGGTGCCTAC CTTCTGGAAT GTCTGTGCCC CAGGTCCTTA GAATGTCTGC 2760
TTCCCGCCGT GGCCAGGACC ACTATTCTCA CTGAGGGAGG AGGATGTCCC AACTGCAGCC 2820
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ATGCTGCTTA GAGACAAGAA AGCAGCTGAT GTCACCCACA AACGATGTTG TTGAAAAGTT 2880
TTGATGTGTA AGTAAATACC CACTTTCTGT ACCTGCTGTG CCTTGTTGAG GCTATGTCAT 2940
CTGCCACCTT TCCCTTGAGG ATAAACAAGG GGTCCTGAAG ACTTAAATTT AGCGGCCTGA 3000
CGTTCCTTTG CACACAATCA ATGCTCGCCA GAATGTTGTT GACACAGTAA TGCCCAGCAG 3060
AGGCCTTTAC TAGAGCATCC TTTGGACGGC GAAGGCCACG GCCTTTCAAG ATGGAAAGCA 3120
GCAGCTTTTC CACTTCCCCA GAGACATTCT GGATGCATTT GCATTGAGTC TGAAAGGGGG 3180
CTTGAGGGAC GTTTGTGACT TCTTGGCGAC TGCCTTTTGT GTGTGGAAGA GACTTGGAAA 3240
GGTCTCAGAC TGAATGTGAC CAATTAACCA GCTTGGTTGA TGATGGGGGA GGGGCTGAGT 3300
TGTGCATGGG CCCAGGTCTG GAGGGCCACG TAAAATCGTT CTGAGTCGTG AGCAGTGTCC 3360
ACCTTGAAGG TCTTC
```

CBF9 Protein sequence

```
Gene name:                   ESTs
Unigene number:              Hs.157601
```

Protein Accession #: none found

```
Signal sequence:             1-17
Transmembrane domains:       none found
VGW domains:                 49-223; 341-518; 529-706
EGF domains:                 298-333; 715-748
Cellular Localization:       plasma membrane
```

```
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MPPFLLLEAV CVFLFSRVPP SLPLQEVHVS KETIGKISAA SKMMWCSAAV DIMFLLDGSN   60
SVGKGSFERS KHFAITVCDG LDISPERVRV GAFQFSSTPH LEFPLDSFST QQEVKARIKR  120
MVFKGGRTET ELALKYLLHR GLPGGRNASV PQILIIVTDG KSQGDVALPS KQLKERGVTV  180
FAVGVRFPRW EELHALASEP RGQHVLLAEQ VEDATNGLFS TLSSSAICSS ATPDCRVEAH  240
PCEHRTLEMV REFAGNAPCW RGSRRTLAVL AAHCPFYSWK RVFLTHPATC YRTTCPGPCD  300
SQPCQNGGTC VPEGLDGYQC LCPLAFGGEA NCALKLSLEC RVDLLFLLDS SAGTTLDGFL  360
RAKVFVKRFV RAVLSEDSRA RVGVATYSRE LLVAVPVGEY QDVPDLVWSL DGIPFRGGPT  420
LTGSALRQAA ERGFGSATRT GQDRPRRVVV LLTESHSEDE VAGPARHARA RELLLLGVGS  480
EAVRAELEEI TGSPKHVMVY SDPQDLFNQI PELQGKLCSR QRPGCRTQAL DLVFMLDTSA  540
SVGPENFAQM QSFVRSCALQ FEVNPDVTQV GLVVYGSQVQ TAFGLDTKPT RAAMLRAISQ  600
APYLGGVGSA GTALLHIYDK VMTVQRGARP GVPKAVVVLT GGRGAEDAAV PAQKLRNNGI  660
SVLVVGVGPV LSEGLRRLAG PRDSLIHVAA YADLRYHQDV LIEWLCGEAK QPVNLCKPSP  720
CMNEGSCVLQ NGSYRCKCRD GWEGPHCENR EWSSCSVCVS QGWILETPLR HMAPVQEGSS  780
RTPPSNYREG LGTEMVPTFW NVCAPGP
```

BFO8 DNA SEQUENCE

```
Gene name:                   TMPRSS3a
Unigene number:              Hs.298241
Probeset Accession #:        AI538613
Nucleic Acid Accession #:    AB038157
Coding sequence:             202-1566 (underlined sequences correspond to start and
                             stop codons)
```

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1          11         21         31         41         51
|          |          |          |          |          |
ACCGGGCACC GGACGGCTCG GGTACTTTCG TTCTTAATTA GGTCATGCCC GTGTGAGCCA   60
GGAAAGGGCT GTGTTTATGG GAAGCCAGTA ACACTGTGGC CTACTATCTC TTCCGTGGTG  120
CCATCTACAT TTTTGGGACT CGGGAATTAT GAGGTAGAGG TGGAGGCGGA GCCGGATGTC  180
AGAGGTCCTG AAATAGTCAC CATGGGGGAA AATGATCCGC CTGCTGTTGA AGCCCCCTTC  240
TCATTCCGAT CGCTTTTTGG CCTTGATGAT TTGAAAATAA GTCCTGTTGC ACCAGATGCA  300
GATGCTGTTG CTGCACAGAT CCTGTCACTG CTGCCATTGA AGTTTTTTCC AATCATCGTC  360
ATTGGGATCA TTGCATTGAT ATTAGCACTG GCCATTGGTC TGGGCATCCA CTTCGACTGC  420
TCAGGGAAGT ACAGATGTCG CTCATCCTTT AAGTGTATCG AGCTGATAGC TCGATGTGAC  480
GGAGTCTCGG ATTGCAAAGA CGGGGAGGAC GAGTACCGCT GTGTCCGGGT GGGTGGTCAG  540
AATGCCGTGC TCCAGGTGTT CACAGCTGCT TCGTGGAAGA CCATGTGCTC CGATGACTGG  600
AAGGGTCACT ACGCAAATGT TGCCTGTGCC CAACTGGGTT TCCCAAGCTA TGTGAGTTCA  660
GATAACCTCA GAGTGAGCTC GCTGGAGGGG CAGTTCCGGG AGGAGTTTGT GTCCATCGAT  720
CACCTCTTGC CAGATGACAA GGTGACTGCA TTACACCACT CAGTATATGT GAGGGAGGGA  780
```

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TGTGCCTCTG GCCACGTGGT TACCTTGCAG TGCACAGCCT GTGGTCATAG AAGGGGCTAC    840
AGCTCACGCA TCGTGGGTGG AAACATGTCC TTGCTCTCGC AGTGGCCCTG GCAGGCCAGC    900
CTTCAGTTCC AGGGCTACCA CCTGTGCGGG GGCTCTGTCA TCACGCCCCT GTGGATCATC    960
ACTGCTGCAC ACTGTGTTTA TGACTTGTAC CTCCCCAAGT CATGGACCAT CCAGGTGGGT   1020
CTAGTTTCCC TGTTGGACAA TCCAGCCCCA TCCCACTTGG TGGAGAAGAT TGTCTACCAC   1080
AGCAAGTACA AGCCAAAGAG GCTGGGCAAT GACATCGCCC TTATGAAGCT GGCCGGGCCA   1140
CTCACGTTCA ATGAAATGAT CCAGCCTGTG TGCCTGCCCA ACTCTGAAGA GAACTTCCCC   1200
GATGGAAAAG TGTGCTGGAC GTCAGGATGG GGGGCCACAG AGGATGGAGC AGGTGACGCC   1260
TCCCCTGTCC TGAACCACGC GGCCGTCCCT TTGATTTCCA ACAAGATCTG CAACCACAGG   1320
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GTGGACAGCT GCCAGGGGGA CAGCGGGGGG CCCCTGGTGT GTCAAGAGAG GAGGCTGTGG   1440
AAGTTAGTGG GAGCGACCAG CTTTGGCATC GGCTGCGCAG AGGTGAACAA GCCTGGGGTG   1500
TACACCCGTG TCACCTCCTT CCTGGACTGG ATCCACGAGC AGATGGAGAG AGACCTAAAA   1560
ACCTGAAGAG GAAGGGGACA AGTAGCCACC TGAGTTCCTG AGGTGATGAA GACAGCCCGA   1620
TCCTCCCCTG GACTCCCGTG TAGGAACCTG CACACGAGCA GACACCCTTG GAGCTCTGAG   1680
TTCCGGCACC AGTAGCAGGC CCGAAAGAGG CACCCTTCCA TCTGATTCCA GCACAACCTT   1740
CAAGCTGCTT TTTGTTTTTT GTTTTTTTGA GGTGGAGTCT CGCTCTGTTG CCCAGGCTGG   1800
AGTGCAGTGG CGAAATCCCT GCTCACTGCA GCCTCCGCTT CCCTGGTTCA AGCGATTCTC   1860
TTGCCTCAGC TTCCCCAGTA GCTGGGACCA CAGGTGCCCG CCACCACACC CAACTAATTT   1920
TTGTATTTTT AGTAGAGACA GGGTTTCACC ATGTTGGCCA GGCTGCTCTC AAACCCCTGA   1980
CCTCAAATGA TGTGCCTGCT TCAGCCTCCC ACAGTGCTGG GATTACAGGC ATGGGCCACC   2040
ACGCCTAGCC TCACGCTCCT TTCTGATCTT CACTAAGAAC AAAAGAAGCA GCAACTTGCA   2100
AGGGCGGCCT TTCCCACTGG TCCATCTGGT TTTCTCTCCA GGGGTCTTGC AAAATTCCTG   2160
ACGAGATAAG CAGTTATGTG ACCTCACGTG CAAAGCCACC AACAGCCACT CAGAAAAGAC   2220
GCACCAGCCC AGAAGTGCAG AACTGCAGTC ACTGCACGTT TTCATCTCTA GGGACCAGAA   2280
CCAAACCCAC CCTTTCTACT TCCAAGACTT ATTTTCACAT GTGGGGAGGT TAATCTAGGA   2340
ATGACTCGTT TAAGGCCTAT TTTCATGATT TCTTTGTAGC ATTTGGTGCT TGACGTATTA   2400
TTGTCCTTTG ATTCCAAATA ATATGTTTCC TTCCCTCAAA AAAAAAAAAA AAAAAAAAAA   2460
AAAAAAAA
```

BFO8 Protein sequence:

```
Gene name:                  TMPRSS3a
Unigene number:             Hs.298241
Probeset Accession #:       AI538613
Protein Accession #:        BAB20077
Signal sequence:            none found
Transmembrane domains:      43-65, 239-261
Tryp_SPc domain:            216-444
Cellular Localization:      not determined
```

```
1          11         21         31         41         51
|          |          |          |          |          |
MGENDPPAVE APFSFRSLFG LDDLKISPVA PDADAVAAQI LSLLPLKFFP IIVIGIIALI    60
LALAIGLGIH FDCSGKYRCR SSFKCIELIA RCDGVSDCKD GEDEYRCVRV GGQNAVLQVF   120
TAASWKTMCS DDWKGHYANV ACAQLGFPSY VSSDNLRVSS LEGQFREEFV SIDHLLPDDK   180
VTALHHSVYV REGCASGHVV TLQCTACGHR RGYSSRIVGG NMSLLSQWPW QASLQFQGYH   240
LCGGSVITPL WIITAAHCVY DLYLPKSWTI QVGLVSLLDN PAPSHLVEKI VYHSKYKPKR   300
LGNDIALMKL AGPLTFNEMI QPVCLPNSEE NFPDGKVCWT SGWGATEDGA GDASPVLNHA   360
AVPLISNKIC NHRDVYGGII SPSMLCAGYL TGGVDSCQGD SGGPLVCQER RLWKLVGATS   420
FGIGCAEVNK PGVYTRVTSF LDWIHEQMER DLKT
```

WHAT IS CLAIMED IS:

1. A method of screening drug candidates comprising:

a) providing a cell that expresses an expression profile gene selected from the group consisting of an expression profile gene set forth in Table 1 or Table 2 or fragment thereof;

b) adding a drug candidate to said cell; and

c) determining the effect of said drug candidate on the expression of said expression profile gene.

2. A method according to claim 1 wherein said determining comprises comparing the level of expression in the absence of said drug candidate to the level of expression in the presence of said drug candidate.

3. A method of screening for a bioactive agent capable of binding to a colorectal cancer modulator protein (colorectal cancer modulator protein), wherein said colorectal cancer modulator protein is encoded by a nucleic acid selected from the group consisting of a nucleic acid of Table 1 or Table 2 or a fragment thereof, said method comprising:

a) combining said colorectal cancer modulator protein and a candidate bioactive agent; and

b) determining the binding of said candidate agent to said colorectal cancer modulator protein.

4. A method for screening for a bioactive agent capable of modulating the activity of a colorectal cancer modulator protein, wherein said colorectal cancer modulator protein is encoded by a nucleic acid selected from the group consisting of a nucleic acid of Table 1 or Table 2 or a fragment thereof, said method comprising:

a) combining said colorectal cancer modulator protein and a candidate bioactive agent; and

b) determining the effect of said candidate agent on the bioactivity of said colorectal cancer modulator protein.

5. A method of evaluating the effect of a candidate colorectal cancer drug comprising:

a) administering said drug to a patient;

b) removing a cell sample from said patient; and

c) determining the expression of a gene selected from the group consisting of a nucleic acid of Table 1 or Table 2.

6. A method according to claim 5 further comprising comparing said expression profile to an expression profile of a healthy individual.

7. A method of diagnosing colorectal cancer comprising:

a) determining the expression of one or more genes selected from the group consisting of a nucleic acid of Table 1 or Table 2 or a fragment thereof or a polypeptide encoded thereby in a first tissue type of a first individual; and

b) comparing said expression of said gene(s) from a second normal tissue type from said first individual or a second unaffected individual;

wherein a difference in said expression indicates that the first individual has colorectal cancer.

8. A method for screening for a bioactive agent capable of interfering with the binding of a colorectal cancer modulator protein (colorectal cancer modulator protein) or a fragment thereof and an antibody which binds to said colorectal cancer modulator protein or fragment thereof, said method comprising:

a) combining a colorectal cancer modulator protein or fragment thereof, a candidate bioactive agent and an antibody which binds to said colorectal cancer modulator protein or fragment thereof; and

b) determining the binding of said colorectal cancer modulator protein or fragment thereof and said antibody.

9. A method for inhibiting the activity of a colorectal cancer modulator protein (colorectal cancer modulator protein), wherein said colorectal cancer modulator protein is encoded by a nucleic acid selected from the group consisting of a nucleic acid of Table 1 or Table 2 or a fragment thereof, said method comprising binding an inhibitor to said colorectal cancer modulator protein.

10. A method according to claim 9 wherein said inhibitor is an antibody.

11. A method of treating colorectal cancer comprising administering to a patient an inhibitor of a colorectal cancer modulator protein, wherein said colorectal cancer modulator protein is encoded by a nucleic acid selected from the group consisting of a nucleic acid of Table 1 or Table 2 or a fragment thereof.

12. A method according to claim 11 wherein said inhibitor is an antibody.

13. A method of neutralizing the effect of a colorectal cancer modulator protein, or a fragment thereof, comprising contacting an agent specific for said protein with said protein in an amount sufficient to effect neutralization.

14. A method for localizing a therapeutic moiety to colorectal cancer tissue comprising exposing said tissue to an antibody to a colorectal cancer modulator protein or fragment thereof conjugated to said therapeutic moiety.

15. The method of Claim 14, wherein said therapeutic moiety is a cytotoxic agent.

16. The method of Claim 14, wherein said therapeutic moiety is a radioisotope.

17. A method for inhibiting colorectal cancer in a cell, wherein said method comprises administering to a cell a composition comprising antisense molecules to a nucleic acid of Table 1 or Table 2.

18. An antibody which specifically binds to a protein encoded by a nucleic acid of Table 1 or Table 2 or a fragment thereof.

19. The antibody of Claim 18, wherein said antibody is a monoclonal antibody.

20. The antibody of Claim 18, wherein said antibody is a humanized antibody.

21. The antibody of Claim 18, wherein said antibody is an antibody fragment.

22. A biochip comprising one or more nucleic acid segments selected from the group consisting of a nucleic acid of Table 1 or Table 2 or a fragment thereof, wherein said biochip comprises fewer than 1000 nucleic acid probes.

23. A nucleic acid having a sequence at least 95% homologous to a sequence of a nucleic acid of Table 1 or Table 2 or its complement.

24. A nucleic acid which hybridizes under high stringency to a nucleic acid of Table 1 or Table 2 or its complement.

25. A polypeptide encoded by the nucleic acid of Claim 23 or 24.

26. A method of eliciting an immune response in an individual, said method comprising administering to said individual a composition comprising the polypeptide of Claim 25 or a fragment thereof.

27. A method of eliciting an immune response in an individual, said method comprising administering to said individual a composition comprising a nucleic acid comprising a sequence of a nucleic acid of Table 1 or Table 2 or a fragment thereof.

28. A method of determining the prognosis of an individual with colorectal cancer comprising:

a) determining the expression of one or more genes selected from the group consisting of a nucleic acid of Table 1 or Table 2 or a fragment thereof in a first tissue type of a first individual; and

b) comparing said expression of said gene(s) from a second normal tissue type from said first individual or a second unaffected individual;

wherein a substantial difference in said expression indicates a poor prognosis.

29. A method of treating colorectal cancer comprising administering to an individual having colorectal cancer an antibody to a colorectal cancer modulator protein or fragment thereof conjugated to a therapeutic moiety.

30. The method of Claim 29, wherein said therapeutic moiety is a cytotoxic agent.

31. The method of Claim 29, wherein said therapeutic moiety is a radioisotope.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 March 2002 (21.03.2002)

PCT

(10) International Publication Number
WO 02/021996 A3

(51) International Patent Classification[7]: G01N 33/53

(21) International Application Number: PCT/US01/28716

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(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
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09/930,020 14 August 2001 (14.08.2001) US

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(72) Inventors; and
(75) Inventors/Applicants (*for US only*): **GISH, Kurt, C.** [US/US]; 40 Perego Terrace #2, San Francisco, CA 94131 (US). **MACK, David, H.** [US/US]; 2076 Monterey Avenue, Menlo Park, CA 94025 (US). **WILSON, Keith, E.** [US/US]; 219 Jeter Street, Redwood City, CA 94062 (US).

(74) Agents: **BASTIAN, Kevin, L.** et al.; Townsend and Townsend and Crew LLP, Two Embarcadero Center, Eighth Floor, San Francisco, CA 94111 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report: 6 February 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/021996 A3

(54) Title: METHODS OF DIAGNOSIS OF COLORECTAL CANCER, COMPOSITIONS AND METHODS OF SCREENING FOR COLORECTAL CANCER MODULATORS

(57) Abstract: Described herein are methods that can be used for diagnosis and prognosis of colorectal cancer. Also described herein are methods that can be used to screen candidate bioactive agents for the ability to modulate colorectal cancer. Additionally, methods and molecular targets (genes and their products) for therapeutic intervention in colorectal and other cancers are described.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/28716

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : G01N 33/53
US CL : 435/7.1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/7.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
MEDLINE: inhibition of antibody binding; colorectal cancer

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SAKURAI et al. Selection of a monoclonal antibody reactive with a high-molecular-weight glycoprotein circulating in the body fluid of gastrointestinal cancer patients. Cancer Research. 15 July 1988, Vol. 48, pages 4053-4058.	8
X	PRICE et al. Mapping of monoclonal antibody-defined epitopes associated with carcinoembryonic antigen, CEA. Cancer Immunology & Immunotherapy. 1987, vol. 25, pages 10-15.	8
X	DATABASE MEDLINE, Accession No. 93302201, KOBAYAHI et al. Basic and clinical studies of serum CA195 antigen assay with "BL-CA195" kit. Kaku Igaku [Japanese Journal of Nuclear Medicine]. April 1993. Vol. 30, No. 4, pp. 441-447 (abstract only;).	8

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 May 2002 (23.05.2002)	28 AUG 2002

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Stephen L. Rawlings, Ph.D. Janice Ford for
Facsimile No. (703)305-3230	Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/28716

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claim Nos.: 1-7, 9-12, and 17-28
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Please See Continuation Sheet

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 8

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/28716

Continuation of Box I Reason 2:
Claims 1-7, 9-12, and 17-28 have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a). More particularly, claims 1-7, 9-12, and 17-28 are drawn to expression profile genes set forth in Table 1 or Table 2 or fragment thereof, but Table 1 does not set forth the sequence of the expression profile genes and while Table 2 sets forth the sequence of the expression profile genes, Table II does not identify the sequences by a sequence identification number that corresponds to the identical sequence contained in the Sequence Listing on the Computer Readable Format. Therefore, the claims could not be searched because the sequences to which the claims refer are not disclosed or cannot be searched.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 8, drawn to a method for screening for a bioactive agent.

Group II, claim(s) 13, drawn to a method for neutralizing the effect of a colorectal cancer modulator or a fragment thereof.

Group III, claim(s) 14-16, drawn to a method for localizing a therapeutic moiety to a colorectal cancer tissue.

Group IV, claim(s) 29-31, drawn to a method for treating colorectal cancer.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Group I is contacting a protein with an antibody in the presence of a bioactive agent to inhibit the binding of the protein to the antibody.

The special technical feature of Group II is contacting a protein with an agent that neutralizes the effect of the protein.

The special technical feature of Group III is exposing a tissue to an antibody conjugated to a therapeutic moiety.

The special technical feature of Group IV is administering to an individual an antibody conjugated to a therapeutic moiety.

Therefore, Groups I-IV do not share the same or corresponding special technical feature so as to form a single general inventive concept.